

ANNALS of SURGERY

A Monthly Review of
Surgical Science and Practice

Edited by

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Official Publication of the American Surgical Association, of the
New York Surgical Society and the Philadelphia Academy of Surgery

CONTENTS

Hemectomy in Purpura Hemorrhagica—*Eldridge L. Eliason, M.D., L. K. Ferguson, M.D., Philadelphia, Pa.*, 801

Tumors of the Sternum—*George J. Heuer, M.D., Cincinnati, Ohio*, 830

Surgical Treatment of Mediastinal Tumors—*Stuart W. Harrington, M.D., Rochester, Minn.*, 843

Cancer Problem in the General Hospital—*Harold L. Foss, M.D., Danville, Pa.*, 857

Temporary Bilateral Abductor Paralysis without Nerve Injury and Tetany following Thyroidectomy—*Herbert A. Bruce, M.D., Toronto, Canada*, 864

Results Obtained in the Treatment of Raynaud's Disease by Sympathetic Neurectomy and in Thrombo-angiitis Obliterans by Desensitization of Peripheral Sensory Nerves—*Arthur W. Allen, M.D., Boston, Mass.*, 867

Results of Operative Treatment of Cancer of the Breast—*Frank S. Mathews, M.D., New York, N. Y.*, 871

When Should Irradiation with Radium or X-ray Precede Operation or be Employed without Operation?—*Joseph Colt Bloodgood, M.D., Baltimore, Md.*, 882

Inoperable and Malignant Tumors—*Willy Meyer, M.D., New York, N.Y.*, 891

Ulceration of Aberrant Gastric Mucosa in Meckel's Diverticulum—*James M. Mason, M.D., George S. Graham, M.D., Birmingham, Ala.*, 893

Clinical Aspects and Treatment of Primary Lymphosarcoma of the Stomach and Intestines—*David Cheever, M.D., Boston, Mass.*, 911

The Fate of the Obstructed Loop in Intestinal Obstruction following an Anastomosis around the Obstruction without Resection—*William L. Estes, Jr., M.D., C. E. Holm, M.D., Bethlehem, Pa.*, 924

Maggots and Osteomyelitis—*Walton Martin, M.D., William G. Heeks, M.D., New York, N. Y.*, 930

Fracture of the Neck of the Femur—*Kellogg Speed, M.D., Chicago, Ill.*, 951

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ANNALS *of* SURGERY

Vol. XCVI

NOVEMBER, 1932

No. 5

TRANSACTIONS AMERICAN SURGICAL ASSOCIATION

MEETING HELD MAY 16, 17 AND 18, 1932; *Continued*

SPLENECTOMY IN PURPURA HEMORRHAGICA

BY ELDRIDGE L. ELIASON, M.D., AND L. K. FERGUSON, M.D.
OF PHILADELPHIA, PA.

PURPURA hemorrhagica or thrombocytopenic purpura is still a medical and surgical problem, although its existence was first noted more than 150 years ago. Despite much work and attention directed towards a solution of its etiology and pathology, the answer is not yet. An attempt is here made to marshall all the information that is available in the literature and to present a critical analysis of this data which analysis gives the numerous theories and a brief description of the work done, in demonstrating the possible etiological factors of this strange disease. The true symptomatology is discussed and a real differential diagnosis urged as an aid in successful treatment. All the available reported cases and five personal cases are presented, while a comparative analysis is made in an attempt to show the value of splenectomy in both the acute and chronic forms and also to demonstrate that the mortality has been appreciably reduced in the last four years, chiefly by reason of proper pre-operative and post-operative transfusions flanking a well-executed splenectomy.

Purpura hemorrhagica was first described by Werlhof,¹⁸ in 1775. Knowledge concerning the nature of the disease developed gradually, until even today there is no complete agreement as to the etiological factors concerned nor as to the mechanism by which these factors act. Denys,²⁵ in 1887, first observed that the blood-platelets were missing in a case of purpura. Nine years later (1896), Hayem⁵⁸ showed that in purpura there was a failure of clot retractility. Duke,²⁹ in 1910, demonstrated that a thrombocytopenia and fibrinogen lack have very definite effects on bleeding time. He pointed out that the reduction of platelets in purpura hemorrhagica is associated with an increased bleeding time, but not with any marked variation in the coagulation time. Hess⁶⁰ showed conclusively that there was a marked weakening of the capillary vessels in purpura hemorrhagica as evidenced by the petechial and even large subcutaneous hemorrhages which developed distal to a tourniquet applied to the upper arm tight enough to obstruct the venous flow.

These findings stimulated an investigation of blood-platelets, especially

concerning their function in maintaining a normal bleeding time, and as to the reason for their decrease in purpura hemorrhagica. It is now fairly well accepted by all workers in hematology that blood-platelets take their origin from the megakaryocytes of the bone-marrow. These cells are also found in the spleen in disease and in embryonic life,^{84, 87} one of the evidences of close relationships between the units of the hemopoietic system.

The normal function of blood-platelets has been investigated both experimentally and clinically. Janeway, Richardson and Park,⁸⁷ in animal experiments, showed that an extract of platelets has a vasoconstrictor action, not found in an extract of any of the other formed elements of the blood nor in platelet free plasma. Hirose⁸⁸ showed that there was a direct proportion between the platelet count and the vasoconstrictor effect of defibrinated blood when brought into direct contact with the surviving carotid of an ox. Brill and Rosenthal¹² presented evidence to show that capillary hemorrhage is normally stopped by the production of small platelet thrombi, and by the contraction of the vessels. The function of the platelets in the production of a retractile clot has been explained by Glanzmann.⁴⁷ Finally, there is evidence^{12, 89} to show that the platelets produce a thromboplastic substance which has a function in the production of a clot.

The cause of the reduction of platelets in purpura hemorrhagica has been the subject of much controversial reasoning and of considerable experimentation. Frank⁴¹ believed that there was a decreased platelet formation, an aplasia or decreased production of megakaryocytes in the bone-marrow caused by a myelotoxin coming from the spleen. He therefore called the disease essential thrombopenia.

Brill and Rosenthal state there is no diminution in the megakaryocytes in the bone-marrow in purpura hemorrhagica but they believe that the fragmentation of the pseudopods does not take place properly because in this disease the platelets are large and irregular and granular in appearance. (This change in the appearance of the platelets in purpura hemorrhagica was noted also by Rockwood and Sheard¹²¹ in a photomicrographical study.) Brill, *et al.*, believed that the spleen is responsible not only for the alteration in the nature and properties of platelets in purpura hemorrhagica but also that it is the site of the destruction of the defective bodies. Krumbhaar⁸⁴ considers it probable that the spleen exerts "some regulatory influence on the megakaryocytes of the bone-marrow, the site of platelet formation." Mills¹⁰¹ is not sure that the spleen is primarily responsible for the alteration of platelets, but suggests that destruction of altered platelets is one of the normal functions of the spleen.

Kaznelson^{72, 73, 74, 75} outlined his opposition to Frank's decreased platelet production theory somewhat as follows: (1) If there were an inhibition of megakaryocyte production there should also be an alteration in other blood-cells formed by bone-marrow. (2) If there were a bone-marrow lesion, how could splenectomy effect an almost immediate cure? (3) The large size of the platelets found in purpura hemorrhagica indicates a stimulation of bone-marrow. He believes that the enlargement of the spleen often found in purpura suggests that that organ may be the site of the platelet destruction. For this reason he named the disease thrombocytolytic purpura and he suggested splenectomy as a means of treatment.

Experimentally, many investigations have shown that the injection of antiplatelet serum and anti-spleen serum decreases the platelets in the circulating blood.^{6, 89} Various toxic and irritating substances when injected into the blood-stream also lower the platelet count.⁹⁰ Most authors now agree that the decrease in platelet content of the blood cannot alone account for the symptoms of hemorrhage produced in purpura hemorrhagica. The belief is general that there is also a lesion of the capillaries,^{6, 12, 16, 100, 119} and that in purpura the entire reticulo-endothelial system is at fault.

Because the spleen is thought to be the organ in which the destruction of the defective platelets takes place, Kaznelson,⁷² in 1916, first suggested splenectomy as a means of

SPLENECTOMY IN PURPURA HEMORRHAGICA

treating these patients. He noted an almost immediate cessation of bleeding and a rapid and marked increase in the number of blood-platelets after extirpation of the spleen. This observation has been confirmed many times since Kaznelson's first case, both experimentally,^{9, 94, 120} and by numerous surgeons who have performed splenectomies for purpura hemorrhagica. Bedson⁹ has shown in guinea-pigs that for three or four weeks after splenectomy while the platelet count is still high, antiplatelet serum has no effect in dosages sufficient to cause fatal purpura in normal control animals. Both experimental and clinical observers have noted a gradual fall after the immediate rise in the number of platelets after splenectomy and during the fall Bedson found his animals normally susceptible to antiplatelet serum.

The question has been raised as to whether the removal of the spleen *per se* is the effective agent in causing the increase in platelets after splenectomy. Holloway and Blackford,⁹⁴ in studying the platelet counts of the splenic artery and the splenic or peripheral veins, failed to bear out the platelet-destroying function of the spleen. Much of the experimental work seems to show that although splenectomy does produce a rapid rise in blood-platelets, other operations of equal magnitude produce similar results. Bachman and Hultgren,³ Liles,⁹⁰ and Steiner and Gunn,¹²⁰ have demonstrated these facts in rabbits and they conclude that "the degree of rise in the platelet count depends upon the amount of trauma sustained by the tissues."

Dawbarn, Erlam and Evans²² found a rise in the platelet count after operation, fractures and child-birth, beginning on the sixth day and reaching a maximum on the tenth. The platelets reached the normal number again in about three weeks. They believe that the common factor is injury to tissue with absorption of the products of protein disintegration. Our own experience has been that there is usually an immediate fall in the platelet count after an operation other than splenectomy. A rather marked rise occurs after about the sixth post-operative day which is maintained for a week or ten days or even longer. Von Goidsenhoven,²⁴¹ in reporting twelve cases of purpura hemorrhagica treated by ligation of the splenic artery, gives platelet counts before and after operation which also show a delayed rise in most cases. It would seem that other operations than splenectomy at least do not produce the immediate marked rise usually noted after removal of the spleen in patients.

It might be expected that by extirpation of the spleen, the surgeon was removing a pathological organ. Gregory²⁴ commonly finds a perisplenitis at operation and suggests that there is a primary infective lesion of the spleen. Leriche and Horrenberger⁹¹ assert that the splenic picture is one of infectious splenomegaly without specific characteristics. Kaznelson⁷² cites splenomegaly as evidence pointing to disease of the spleen in purpura hemorrhagica. On the other hand, MacCarty⁹⁸ has studied twenty spleens removed surgically because of purpura hemorrhagica. He says he has "not been able to distinguish this type of spleen from any normal spleen." The numerous reports from the literature fail to show any constant or characteristic histological changes in the spleen in purpura. That splenomegaly is not a characteristic finding is shown by McLean, *et al.*,⁹⁹ and by Stewart.¹³¹ McLean, Kreidel and Caffey were able to palpate the spleen in only five of their twenty-one children with purpura hemorrhagica. Stewart, in reviewing thirty-five cases reported, noted fifteen with enlarged or palpable spleens and eleven with non-palpable or normal spleens.

From the foregoing it must be concluded that although many operators have repeated the brilliant results obtained by Kaznelson in his cases of purpura hemorrhagica with splenectomy there is still no definite evidence that the spleen is the organ at fault in this disease. Clinical experience bears out the various experimental investigations to point toward a dysfunction of the whole hemopoietic system.

In spite of the fact that the spleen cannot be definitely incriminated as

the seat of the disease in purpura hemorrhagica, the good results which have followed its removal have led many surgeons to accept this method of treatment. There appears to be an almost universal agreement that splenectomy is indicated if the diagnosis is definitely established, and if the case is one of the chronic recurring type.

The diagnosis is made on the following points: (1) "Spontaneous extravasation of blood into or under the skin and mucous membranes of the body."¹¹⁷ (2) Diminished platelet count. (3) Prolonged bleeding time. (4) Approximately normal coagulation time. (5) Absence of clot retraction. (6) The appearance of petechia in the skin distal to a tourniquet blocking the venous but not the arterial flow. (7) Secondary anæmia without constant changes in the red blood-cells. (8) No constant variation in the white blood-cells, but usually an increase rather than a decrease.

Hitzrot⁸⁸ points out that the differential diagnosis must be made from hemophilia and anaphylactic purpura. The diagnosis from hemophilia may be made on the basis of the non-traumatic origin of the bleeding, the lack of a familial history, the normal clotting time, the prolonged bleeding time, and the decrease in platelets. The anaphylactic type of purpura is usually associated with fever. It is preceded by premonitory symptoms and does not show the prolonged bleeding time or absence of clot retraction associated with purpura hemorrhagica.

In addition, the diagnosis must be made between purpura hemorrhagica and two other hemorrhagic diseases, acute aplastic anæmia and acute leukæmia. In acute aplastic anæmia with hæmorrhage, there is a marked diminution of all the former elements of the blood. There is an absence of reticulated red cells and usually a decided leukopenia whereas in purpura hemorrhagica a moderate leucocytosis is the rule. The acute leukæmia with a normal white blood count is perhaps the hardest differential diagnosis to make. The chief diagnostic point appears to be the relative marked increase of the young white cells in the blood in leukæmia. Several reports in the literature describe cases in which splenectomy was performed for purpura hemorrhagica in which there was later developed the typical picture of acute leukæmia.

With these diagnostic criteria in mind it may be well to consider the second point in the indications for splenectomy, *viz.*: the chronicity of the case. Whipple¹³⁰ classes as chronic those cases of purpura hemorrhagica having repeated attacks of petechia, purpuric areas, bleeding from the gums and menorrhagia in women. The bleeding is not usually very profuse and is not into the alimentary canal or into the parenchyma of organs. He is of the opinion that in these cases the major portion of the disturbance in the reticulo-endothelial system is in the spleen because splenectomy produces a cure. Splenectomy is therefore advised in the chronic case. In this opinion he is supported by Spence,¹²⁸ Fitz Hugh,⁸⁹ Jones,⁷¹ and many others. Williamson¹³⁸ limits his indications for splenectomy to his chronic cases in which the severity of the disease interferes with the normal life of the patient, making the patient a chronic invalid, or to those cases in which the severity and frequency of the hæmorrhages endanger the life of the patient.

The so-called acute purpura hemorrhagica is not so well defined in the literature. Some writers denote by the acute type the patient who suddenly begins to bleed without any previous history of hæmorrhage. Williamson¹³⁸ believes splenectomy is contra-indicated in the first attack, both on account of the uncertainty of the diagnosis and because of the unfavorable results.

Other authors such as Whipple¹³⁰ define the acute type as purpura hemorrhagica, occurring without any previous history of hæmorrhage, in which there is "sudden, severe, uncontrollable oozing of blood from mucous membranes and into the subcutaneous tissues and the internal organs." Hematemesis, hematuria, melæna and diffuse menor-

SPLENECTOMY IN PURPURA HEMORRHAGICA

rhagia are characteristic symptoms. Whipple believes that such cases should be tided over by transfusions until the bleeding has stopped; and when built up, splenectomy to prevent recurrence. Still other writers designate those cases as acute in which there is uncontrollable severe hæmorrhage without reference to the number of previous attacks.

The opinions with regard to splenectomy in the so-called acute stage of the disease are varied. Fitz Hugh³⁸ and Jones⁷¹ give the clinician's view in expressing the opinion that splenectomy has seemed to only hasten the fatal outcome in the acute fulminating cases. Whipple¹³³ and Spence¹³⁸ on the basis of their case analyses believe splenectomy is definitely contra-indicated in these cases. Giffin,⁴⁶ Reuben and Claman,¹¹⁹ Rankin and Anderson,¹¹⁷ Cowen,¹⁹ Kerlin,⁷⁸ and Litchfield⁹⁶ all conclude that the acuteness of the hæmorrhage is not a safe guide as to whether splenectomy is indicated. These writers recognize that the results of splenectomy are much better in the chronic recurring type of purpura hemorrhagica with the hypertrophied spleen, but they hold to the view that even in the face of acute hæmorrhage, splenectomy should be performed if repeated transfusions fail to arrest bleeding, notwithstanding the fact that an occasional fatality may result. Maingot¹⁰⁶ is even more outspoken. He believes that splenectomy is the correct treatment for all cases of essential thrombopenic purpura hemorrhagica whether of the acute or of the chronic relapsing types. He maintains "that it is more urgently indicated for the acute types because medical treatment, blood transfusions, etc., have no effect in arresting or even in ameliorating the factors which determine the fatal outcome."

A study of a group of cases of purpura hemorrhagica and of the literature on the subject leads to a view that the disease is one whose chief danger is from hæmorrhage, the exact etiological mechanism of which is not known. The disease tends to a spontaneous cure and recurrence as is characteristic of many of the blood dyscrasias. The therapeutic indications would appear to be, first, control of the hæmorrhage, and second, attempts to remove the etiological factors.

It would appear, therefore, that the treatment of hemorrhagica purpura cannot be divided into that for the acute type and that for the chronic type. The more logical consideration of the therapy would seem to be to employ first the most conservative method of treatment which removes the danger of immediate severe or recurrent hæmorrhage.

There can be no doubt that repeated transfusions may be effective in stopping the hæmorrhage and in producing a remission, often without subsequent recurrence, in many cases of purpura hemorrhagica. Larrabee,⁸⁰ Jones,⁸⁰ Krasso,⁸² Engel,⁸³ and Moffatt¹⁰⁰ report proven cases which support this view. McLean, *et al.*,⁹⁰ have recently reported eight patients, all children, treated by transfusion. Of these five acute and three chronic cases, there were no deaths, five were symptom free, four to fourteen months, and three were still under treatment.

Larrabee believes that a transfusion of 500 to 600 cubic centimetres of unmodified blood raises the platelet count 20,000. He thinks the effect is approximately one week in duration, the life of the platelets in the blood-stream. Although this may be a useful measure in many of the less severe cases, transfusion alone usually does not prove sufficient in most of the patients with extensive hæmorrhage. Other methods of controlling hæmorrhages in purpura should be mentioned in this connection. Many of them have proved successful in an occasional case but their very multitude suggests that they have not been universally effective. Calcium administration or an elevation of the blood calcium by parathormone is recommended by some authors.⁷¹ Dixon⁷⁷ reports four cases treated by intramuscular injections of twenty to thirty cubic centimetres of autogenous blood. Liver extract or a liver diet has been used with success by a few authors.^{71, 90} Pancoast, Pendergrass and Fitz Hugh¹⁰⁰ have reviewed the literature and reported their results with the Röntgen treatment of purpura. Ultra-violet radiation has been shown to effect an increase in the platelet count experimentally,¹³⁰ and this finding has been used clinically by Giffin,⁴⁶ Jones,⁷¹ McLean, *et al.*,⁹⁰ and many others.

A diet high in Vitamins B and C has been employed.^{44, 71} Thromboplastin injections have been given by many in the therapy of purpura.⁷¹ Antivenin injections have proved advantageous in other hands. The reports are increasing of the treatment of purpura with various forms of non-specific protein shock. Horse serum, milk, coagulen, peptone and even salvarsan have been given intramuscularly or intravenously with some reports of successful cases.^{20, 26, 210, 46} None of these methods appears to produce the rapid control of bleeding necessary in the patient with extensive hæmorrhage. The most effective method of producing an immediate or rapid hemostasis appears to be the removal of the spleen. Whether an etiological factor in the causation of purpura is thereby removed, or whether the tissue trauma incidental to the operation is the effective factor in raising the blood-platelets and in stopping the hæmorrhage, the fact remains that no other procedure gives such striking results. Our own experience has been similar to that of most other operators, that the previous uncontrollable bleeding often stops almost entirely within the first twenty-four to forty-eight hours after operation, coincidental with a sharp rise in the platelet count.

Uncontrollable bleeding, then, whether sudden and severe or recurrent, appears to be the indication for splenectomy in purpura hemorrhagica.

When should the operation be performed? The splenectomy should be performed before the patient has bled to such an extent as to be a poor operative risk, or after the patient has been prepared for operation by adequate blood transfusions. In some cases the hæmorrhage is so marked that a decision for operation must be made without delay. Anschütz² reports a case in which the hæmoglobin and red cells dropped from 85 per cent. and 4,100,000 to 45 per cent. and 2,460,000 in two hours. Immediate operation and transfusion saved the patient. In other instances less rapid but continuous bleeding may so deplete the patient as to make him a poor operative risk. In such cases repeated transfusions should be given until the hæmoglobin is returned to at least 50 per cent. (Marsh⁹⁷ points out that in six of the early fatal cases of splenectomy in "acute" purpura hemorrhagica the hæmoglobin and blood count were low, and that in all of the successful cases up to 1930 transfusions were given before operation.)

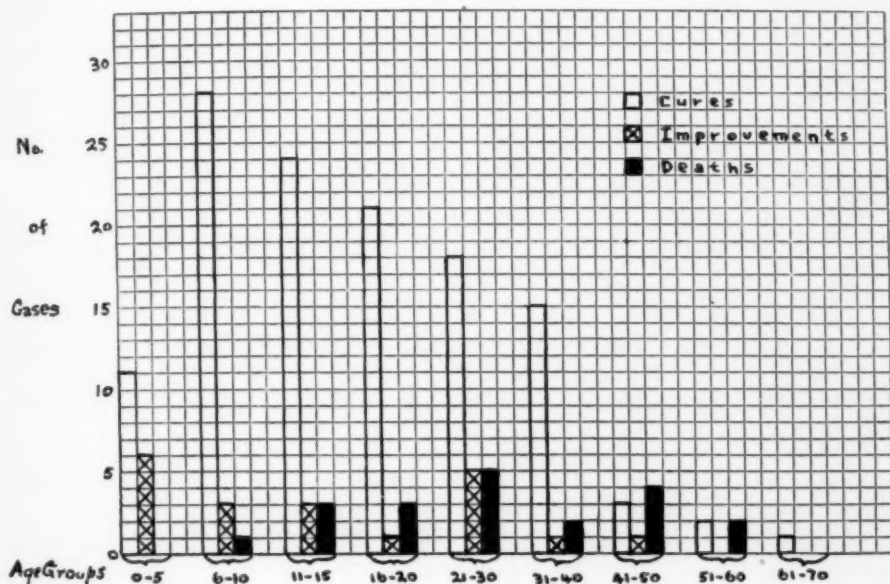
When the patient has been properly prepared, splenectomy may usually be performed without the danger of death from post-operative shock, the probable cause of the fatal outcome in many of the early cases.

The influence of the age of the patient at the time splenectomy is performed is frequently mentioned in the literature. Stewart,¹³¹ Anschütz,² and Washburn¹³⁵ agree that the results are more satisfactory in children than in adults, and Washburn suggests further that the prognosis after splenectomy is probably more favorable if the spleen is removed early in the course of the disease. These statements are in agreement with Gross's⁵⁵ findings that the spleen is most active in the young and least active in the old. It would seem that early splenectomy or splenectomy in the early years might be expected to give the best results if the spleen plays a part in the disease. (See chart.)

The second indication in the treatment of purpura hemorrhagica would appear to be to remove the etiological factors. This is truly a real problem at this time when there is no definite knowledge concerning the cause of the

SPLENECTOMY IN PURPURA HEMORRHAGICA

disease. However, it has been shown experimentally that purpura-like states, with marked reduction of the blood platelets, may be induced by the injection of diphtheria or other toxins.³⁰ Considerable literature is developing concerning the occurrence of purpura hemorrhagica after the injections of arsenicals in the treatment of syphilis.^{94, 68, 23, 134, 9, 11} Whipple¹³⁶ showed that in twelve of twenty-one children with purpura definite infections preceded the onset of the disease. He suggests that thrombocytopenia may be an allergic manifestation affecting particularly the megakaryocytes. Stewart¹³¹ points out that bacterial toxins may stimulate the reticulo-endothelial system to an increased destruction of platelets, and he believes it is important, therefore, to remove foci of infection in order to prevent recurrences.



Graph showing the frequency of purpura according to age in 163 patients. Note that there is a decrease in the number of cases in the older age groups and a relative increase in post-operative fatalities.

Giffin⁴⁴ believes that splenectomy should be performed first before attempting to remove the focal infections and he concludes with the statement that he knows "of no instance in which recurrence of petechial or purpuric areas has persisted following careful elimination of foci."

The weight of evidence, therefore, points to some type of toxæmia as an etiological factor in production of purpura hemorrhagica. The logical prophylactic treatment is to remove the foci of infection after control of the hæmorrhage has been accomplished.

We are reporting herewith five cases of purpura with splenectomy, two of which were of the so-called acute type.

CASE I.—A. M. W., female, twelve years old, admitted to the service of Doctor Riesman, Philadelphia General Hospital, February 11, 1930. She complained of continuous bleeding from the nose since February 9, 1930. Packing did not control the

bleeding. There was slight oozing of blood from the navel and rather profuse bleeding from the gums. Ecchymoses were found under the conjunctiva, in the fundus of the eye and over the extremities. Many petechia were found in the skin and mucous membranes of the mouth. The skin showed a definite pallor. The Hess capillary resistance test was positive. The spleen was not palpable. Temperature, 98.6°; pulse, 136; respirations, 24; blood-pressure, 102/40. Blood.—Red blood-cells, 1,800,000; hæmoglobin, 33 per cent.; reticulated red cells, 3 per cent.; white blood-cells, 10,500; polymorphonuclears, 80 per cent.; lymphocytes, 16 per cent.; mononuclears, 4 per cent. Platelets, 40,000. Bleeding time, thirteen minutes. The clot did not retract.

A diagnosis of thrombopenic purpura hemorrhagica was made. Two injections of ten cubic centimetres of thromboplastin were given. Nasal packing was inserted.

February 12, 1930.—Nasal packing changed. Röntgen deep therapy over spleen, 20 per cent. erythema dose. Transfusion 500 cubic centimetres citrated blood. Bleeding constantly.

February 13, 1930.—Temperature, 100°; pulse, 140; respirations, 25. Continuous hæmorrhage from nose and gums. Vomiting blood. Patient rapidly growing weaker. 4 P.M.—Splenectomy, 500 cubic centimetres blood given by transfusion during the operation. The bleeding from the nose stopped during the operation and transfusion. Pulse at end of operation, 120. 10 P.M.—No further signs of hæmorrhage.

February 14, 1930.—No further hæmorrhage. Red blood-cells, 2,750,000; platelets, 160,000.

February 15, 1930.—Transfusion 300 cubic centimetres citrated blood.

February 16, 1930.—Slight bleeding from nose for short time after child had "picked" her nose.

February 17, 1930.—Red blood-cells, 3,550,000; hæmoglobin, 63 per cent.; white blood-cells, 18,000; platelets, 125,000.

February 24, 1930.—Red blood-cells, 3,460,000; hæmoglobin, 65 per cent.; white blood-cells, 8,400; platelets, 120,000.

March 9, 1930.—Wound healed. No further bleeding. Patient discharged. Red blood-cells, 3,500,000; platelets, 160,000.

June 11, 1930.—No recurrence of bleeding. Patient has gained much weight. Red blood-cells, 5,530,000; hæmoglobin, 100 per cent.; white blood-cells, 17,700; platelets, 70,000.

December 3, 1930.—Symptom-free. No recurrence of bleeding. Weight, 116½ pounds. Red blood-cells, 4,610,000; hæmoglobin, 100 per cent.; white blood-cells, 13,850; platelets, 230,000.

June 20, 1931.—No recurrence. Weight 125½ pounds. Red blood-cells, 4,310,000; white blood-cells, 12,400; hæmoglobin, 90 per cent.; platelets, 100,000.

May 10, 1932.—No recurrence. Weight 154 pounds. Bleeding time, two minutes. Red blood-cells, 4,550,000; white blood-cells, 13,600; hæmoglobin, 90 per cent.; platelets, 260,000.

CASE II.—M. G., male, seven years old, admitted to Doctor Lowenburg's service at the Mt. Sinai Hospital, Philadelphia, June 16, 1930, complaining of "blue marks on the body." He had noticed the spots for about three years and they did not always follow trauma. Until his tonsillectomy three years before admission he had had frequent cold and "sore throat." Temperature, 99.6°; pulse, 90. The child was markedly emaciated. The cervical glands were enlarged. There were submucous hæmorrhages on his cheeks, tongue, and pharynx, and multiple petechia and ecchymoses on the trunk and extremities. The spleen was just palpable. Blood.—Red blood-cells, 4,700,000; hæmoglobin, 80 per cent.; platelets, 250,000. Coagulating time, 4½ minutes. Bleeding time, 19 3/8 minutes. Friable, non-retracted clot after twenty-four hours.

July 3, 1930.—Bleeding not marked but has not entirely stopped. Red blood-cells,

SPLENECTOMY IN PURPURA HEMORRHAGICA

4,490,000; hæmoglobin, 80 per cent.; platelets, 140,000. Bleeding time, thirty-one minutes.

July 10, 1930.—Splenectomy.

July 31, 1930.—Recovery uneventful. All bleeding ceased. Discharged. Platelets, 210,000. Bleeding time, 2½ minutes. Solid retracted clot.

January, 1931.—Purpuric spots reappeared and bleeding from gums was noted.

February 17, 1931.—Readmitted. Red blood-cells, 4,490,000; hæmoglobin, 80 per cent. Coagulation time, five minutes. Bleeding time, nine minutes. Platelets, 160,000.

February 23, 1931.—Blood transfusion. Ultra-violet light exposure. Petechia appeared on extremities and chest after confusion. March 3, 1931.—Petechia clearing up. Platelets, 130,000. Calcium gluconate daily. March 23, 1931.—Improving. Bleeding time, 2 1/3 minutes. Platelets, 140,000. March 28, 1931.—Discharged.

April 28, 1931.—No bleeding since discharge from hospital but his mother says "he bruises easily." Red blood-cells, 4,780,000; hæmoglobin, 85 per cent.; white blood-cells, 14,700; polymorphonuclears, 70 per cent.; lymphocytes, 29 per cent.; large mononuclears, 1 per cent. Coagulation time, three minutes. Bleeding time, eighteen minutes. Platelets, 120,000. No solid clot after eighteen hours at 37° C. This patient suffers from frequent upper respiratory infections and probably has a focus of infection in the nose or sinuses, which has not been cleared up.

CASE III.—R. C., female, thirty-three years old, was admitted to the service of Doctor Jump at the Philadelphia General Hospital, April 17, 1931, complaining of bleeding from the gums and vagina. For the past four years her periods had gradually become more profuse. In December, 1930, she was forced to stop her work because of bleeding from mucous membranes. Since April 10, 1931, she had bled from the gums and vagina. She was so weak that she had to come to the hospital. She gave a history of rheumatism in 1923 and of profuse bleeding following the extraction of teeth. There was no familial tendency to bleed. There was continuous bleeding from the gums and large areas of submucous hæmorrhage on the tongue and mucosa of the mouth. The nose contained clots. Petechia were evident in the mucous membranes, conjunctiva and skin. The vagina was pale. There were several hæmorrhagic areas on the labia. When the labia were separated about two ounces of liquid blood escaped. The uterus and vagina failed to show any ulcerations or neoplasm. Large ecchymotic areas were found on the right thigh. Red blood-cells, 2,040,000; hæmoglobin, 30 per cent.; white blood-cells, 7,400; platelets, 40,000. Coagulation time, four minutes. Bleeding time, fifteen minutes +.

April 18, 1931.—450 (c.c.) citrated blood by transfusion. Antivenin ten cubic centimetres intravenously and ten cubic centimetres intramuscularly. Calcium lactate given by mouth in large doses. Bleeding not checked by these measures.

April 20, 1931.—Red blood-cells, 1,900,000; hæmoglobin, 31 per cent.; white blood-cells, 7,900; platelets, 40,000. Bleeding has decreased. April 23, 1931.—Bleeding stopped entirely. Red blood-cells.—1,190,000; hæmoglobin, 30 per cent.; white blood-cells, 16,900; platelets, 320,000.

May 3, 1931.—No further bleeding. Red blood-cells, 2,140,000; hæmoglobin, 40 per cent.; white blood-cells, 9,700; platelets, 350,000.

May 10, 1931.—Bleeding began again from gums. Thromboplastin, twelve cubic centimetres intramuscularly.

May 11, 1931.—Bleeding from gums, nose and vagina. Red blood-cells, 2,380,000; hæmoglobin, 50 per cent.; platelets, 80,000. Bleeding time, twenty-seven minutes. Patient desensitized to antivenin and given ten cubic centimetres intramuscularly.

May 12, 1931.—Profuse bleeding continues. Splenectomy and transfusion.

May 13, 1931.—Bleeding from mucous membranes has stopped. Red blood-cells, 2,640,000; white blood-cells, 17,600; platelets, 210,000. Bleeding time, five minutes.

May 14, 1931.—Slight vaginal bleeding, may be old blood. Red blood-cells, 1,420,000; hæmoglobin, 35 per cent.; platelets, 350,000. Bleeding time, three minutes.

May 17, 1931.—No further bleeding. Purpuric areas are disappearing. May 25, 1931.—Bleeding time, one minute. June 4, 1931.—No further bleeding. Red blood-cells, 3,170,000; platelets, 350,000. We have been unable to locate this patient.

CASE IV.—M. T., male, aged twenty years, was admitted to the service of Doctor Stengel, University Hospital, Philadelphia, February 6, 1931, complaining of bleeding from nose. He has had frequent nose bleeds since he was ten years old. His present attack began one week before his admission and could not be controlled by nasal packing. He had never noted any unusual bleeding from cuts or bruises and there was no familial history of bleeding. At the time he was examined there was continuous bleeding from his nose and gums, and petechia were evident in the skin and mucous membranes. Red blood-cells, 3,300,000; white blood-cells, 24,000; hæmoglobin, 56 per cent.; platelets, too few to count. Bleeding time, $2\frac{1}{2}$ minutes. Coagulation time, five minutes. Slightly retracted clot in twenty-four hours. Tourniquet test, positive.

February 7, 1931.—Patient developed an otitis media of the right ear from which pus is draining.

February 10, 1931.—Still bleeding. Transfusion 500 cubic centimetres citrated blood, fifty cubic centimetres whole blood injected intramuscularly. Platelets, 16,000.

February 11, 1931.—Splenectomy and transfusion. Platelets, 9,200. February 12, 1931.—Still oozing slightly from the nose. Transfusion 500 cubic centimetres.

February 16, 1931.—Slight bleeding from nose. Platelets, 15,000. Bleeding time, $2\frac{1}{2}$ minutes. Slight clot retraction. Transfusion 350 cubic centimetres.

February 28, 1931.—Transfusion 500 cubic centimetres. Still slight bleeding from nose. March 13, 1931.—Platelets, 51,200. Still same ooze from right nostril. Ear is improved. March 23, 1931.—Violent nose bleed today. Platelets, 3,000. Antivenin given intramuscularly. March 26, 1931.—Nasal bleeding slight. Petechia have appeared in the skin of the trunk and extremities. Platelets, 57,600. April 7, 1931.—Patient has had slight bleeding from the nose for past five days. Platelets, 48,000. April 20, 1931.—No bleeding. Patient signed his release from hospital. Platelets, 16,800. May 18, 1931.—No further bleeding. Platelets, 22,400.

May 8, 1932.—Slight epistaxis on two occasions. Working daily. Red blood-cells, 5,100,000; hæmoglobin, 90 per cent.; white blood-cells, 6,800; platelets, 110,400. Bleeding time, one minute.

CASE V.—R. V., male, aged two years, seven months, was admitted September 30, 1931, to the Pædiatric Service, University Hospital, Philadelphia, complaining of blue marks on the skin. He had been normal until the week before admission when bluish spots appeared on the epigastrium and on the legs. Petechia were present on the face and neck. There was a small subconjunctival hæmorrhage in the left eye. The teeth were markedly carious. Hæmorrhages were noted in the hard and soft palate. Red blood-cells, 4,800,000; hæmoglobin, 75 per cent.; white blood-cells, 15,000; platelets, 2,500. Bleeding time, one hour. Clotting time, seven minutes. No clot retraction in seventeen hours.

October 2, 1931.—Platelets, 3,200. Transfusion, 200 cubic centimetres. Platelets after transfusion, 8,000. October 3, 1931.—Platelets, 28,000. Some blood in stool. October 5, 1931.—Platelets, 18,000. Transfusion, 140 cubic centimetres. Large purpuric area on the lateral aspect of left thigh. Whole blood five cubic centimetres given intramuscularly every third day. October 7, 1931.—Platelets, 12,800; red blood-cells, 4,000; hæmoglobin, 100 per cent.

October 9, 1931.—Splenectomy. Spleen very small. Transfusion 100 cubic centimetres. Post-operative blood, red blood-cells, 5,200,000; white blood-cells, 41,400; hæmoglobin, 90 per cent.; Platelets, 38,400. October 10, 1931.—Platelets, 234,000. October 12, 1931.—Platelets, 896,000. October 14, 1931.—Platelets, 540,000. October

SPLENECTOMY IN PURPURA HEMORRHAGICA

22, 1931.—Platelets, 326,000. November 4, 1931.—Platelets, 672,000. Bleeding time, 2½ minutes. No further bleeding since operation. Discharged.

November, 1931.—Tonsillectomy and teeth extraction. No undue bleeding. April 27, 1932.—No bleeding since operation. Patient has gained eight pounds in weight. Red blood-cells, 4,000,000; hæmoglobin, 78 per cent.; white blood-cells, 11,900; platelets, 330,000. Bleeding time, 1½ minutes. Clot retractility, normal. Clotting time, ten minutes.

In order to have some basis on which to judge the results and dangers of splenectomy in purpura hemorrhagica we have collected and analyzed all of the cases we were able to find in the literature up to 1932. The two previous analyses of cases were those of Whipple in 1926¹³⁶ of eighty-one cases and of Spence in 1928¹²⁸ of 101 cases. In Spence's report the case of Farley and of Lee is the same patient making 100 cases reported by Spence. He also included all but five of Whipple's eighty-one cases, so that the combined reports of Whipple and Spence contain 105 individual cases. We have collected an additional 103 cases from the literature and are adding five unreported cases of our own, making a total of 213 cases upon which our analysis has been made. The data have not always been available for a complete analysis and in such instances the figures given are based on the cases in which the significant data have been found.

The cases have been divided into the conventional chronic and acute types in order that our figures may be comparable to the previous reports. Of the 213 cases, thirty-five were classified as acute, 160 as chronic and in eighteen cases it was impossible to classify the type of purpura.

Results.—Of the 213 patients, twenty-eight died as a result of or shortly after operation, a mortality for the whole group of 13.1 per cent. Spence reported 100 cases with twenty deaths, a mortality of 20 per cent. In the 113 additional cases there were only eight deaths, a reduction in the period 1928 to 1932 to 7.08 per cent. The results in the remaining patients may be classified as follows:

"Cures"	156 cases	73.2%
Improved	17 cases	8.0%
Unimproved	6 cases	2.8%
Result unknown	6 cases	2.8%

Cases were classified as cured if they had recovered from their operations and had no further bleeding up to the time when the report was made. This may not be a true picture of the results because at least forty-seven cases were reported within six months from the time of operation, and twenty-eight more between six months and a year after splenectomy. The remaining cases were reported as follows:

1 to 2 years after splenectomy	26 cases
2 to 3 years after splenectomy	12 cases
3 to 4 years after splenectomy	3 cases
4 to 5 years after splenectomy	12 cases
Over 5 years after splenectomy	5 cases
Unknown time after splenectomy	24 cases

ELIASON AND FERGUSON

To date there have been no large series of cases reported from which it is possible to evaluate the five-year results.

Results in Acute Purpura Hemorrhagica

Acute purpura	35 cases	
Cures	22 cases	} 65.7%
Improvement	1 case	
Deaths	12 cases	
		34.3%

These figures are at variance with those of Whipple and Spence. Whipple reported seven deaths in the eight cases of acute purpura with splenectomy, and Spence found ten deaths in twelve cases operated upon, a mortality of 83.3 per cent. Since his report there have been twenty-two cases of acute purpura with only three deaths, a mortality of only 13.6 per cent. in the cases reported since 1928. This figure approaches the mortality figures in chronic purpura. It is probable that the decrease in mortality noted in the above figures may be attributed to a tendency to earlier splenectomy and especially to an improvement in the preparation of these patients for operation.

Results in Chronic Purpura Hemorrhagica

Chronic purpura	160 cases	
Cures	124 cases—77.5%	} 88.1%
Improved	17 cases—10.6%	
Unimproved	4 cases—2.5%	
Deaths	11 cases—7.0%	
No follow-up	4 cases—2.5%	

In Whipple's report there were seventy-three chronic cases, of which six died, a mortality of 8.2 per cent. Spence found a mortality of 11.8 per cent. There has been, therefore, also a reduction in the mortality figures for splenectomy in chronic purpura during the period 1928 to 1932.

Results in Unclassified Purpura Hemorrhagica

Total cases	18
Cures	10 cases—55.5%
Improved	1 case
Deaths	5 cases—27.8%
No follow-up	2 cases

If it were possible to accurately classify these cases, it would naturally increase slightly the mortality figures for the so-called acute and chronic cases.

In investigating the cause of death, it was found that all but one of the acute cases died either on the operating table or on the day of operation. There was one patient who lived until the tenth post-operative day. The factor of delay in operation, and markedly decreased red blood-cells and hæmoglobin was evident in all but two cases, and in these cases the last blood studies given were those several days or more before operation, so that it is probable that these patients too were well bled out at the time of operation.

SPLENECTOMY IN PURPURA HEMORRHAGICA

The deaths in the so-called chronic cases may be grouped under four chief heads: Operative shock, delayed operation, three cases; post-operative intracranial hæmorrhage, three cases; operative accident or post-operative complications, three cases; splenectomy in atypical cases, two cases. Both of the latter cases died some time after operation with the typical picture of aleukæmic leukæmia.

The cases of unclassified purpura died from the same causes: three from operative shock, one three months after operation and from myelogenous leukæmia, and one from cerebral hæmorrhage. In summarizing the causes of death after splenectomy for purpura hemorrhagica, it appears that the most frequent factor is a controllable one, post-operative shock in an anæmic patient. This cause of death appeared evident in eighteen of the twenty-eight fatal cases. Intracranial hæmorrhage led to a fatality in four cases. Operative accidents or complications occurred in three cases and in three cases there was probably an error in diagnosis.

SUMMARY

(1) A review of the literature points to the fact that purpura hemorrhagica is a disease causing not only a reduction of blood-platelets but also a disturbance of the entire reticulo-endothelial system.

(2) It has not yet been proven that the spleen is the organ at fault in purpura hemorrhagica.

(3) A definitely established diagnosis must be made before splenectomy should be considered.

(4) Once the diagnosis is established, the therapeutic indications appear to be (1) control of hæmorrhage, (2) removal of etiological factors.

(5) Splenectomy appears to be the most effective method of controlling extensive hæmorrhage in purpura hemorrhagica of either the acute or recurring type.

(6) Early operation and adequate preparation of the patient by transfusion is imperative.

(7) Removal of foci of infection is the best prophylaxis against recurrences.

(8) Five additional cases of purpura hemorrhagica with splenectomy are reported.

(9) A review of the results obtained in 213 reported cases has been made.

(10) The operative mortality for the whole group was 13.1 per cent. but in the cases collected from the last four years the mortality is only 7.08 per cent. in 113 cases.

(11) In acute purpura, there were thirty-five cases treated by splenectomy with twelve deaths, 34.3 per cent. In the last twenty-two cases there were only three deaths, 13.6 per cent.

(12) In the chronic purpuras there were 160 cases with eleven deaths, 7 per cent.

(13) In eighteen of the twenty-eight cases the cause of death appeared to be post-operative shock in a poor-risk patient; less frequent causes were intracranial hæmorrhage, operative accidents or post-operative complications or incorrect diagnoses.

(14) One hundred eight cases are collected and analyzed.

SUMMARIES OF REPORTED CASES OF SPLENECTOMY FOR THROMBOCYTOPENIC
PURPURA HEMORRHAGICA

(Not including the eighty-one cases reported by Whipple in 1926
or the 101 cases reported by Spence in 1928)

CASE I by Fitz Hugh,⁸⁷ 1925. Female, eight years, chronic (three months). Red blood-cells, 3,600,000; hæmoglobin, 52 per cent.; bleeding time, 8 to 30 minutes; platelets, 6,000 to 30,000. X-radiation and sterilized-milk injections did not produce remission. After splenectomy, bleeding time, 1¼ minutes; platelets, 74,000 to 273,000. No further bleeding but clot remained non-retractile. Reported four months after splenectomy. Cure.

CASE II by Beer,⁷ 1926. Male, fifteen years, chronic (3½ years). Red blood-cells, 2,010,000; hæmoglobin, 28 per cent.; bleeding time, 4½ minutes; platelets, 10,000 to 24,000. X-radiation and transfusions before operation. After splenectomy, bleeding time, three minutes; platelets, 22,000 to 4,000. Slight oozing from wound stopped on tenth post-operative day. Retraction of clot returned. Reported four years after splenectomy. Cure.

CASE III by Beer,⁷ 1926. Female, seventeen years, chronic (nine months). Red blood-cells, 5,120,000 to 2,010,000; hæmoglobin, 94 to 69 per cent.; bleeding time, forty-two minutes; platelets, 10,000. Transfusions and radiotherapy before operation. After splenectomy, bleeding time, seven to two minutes; platelets, 12,000 to 80,000. Bleeding from uterus two weeks after operation. Checked by radiotherapy. Reported two years after splenectomy. Cure.

CASE IV by Beer,⁷ 1926. Male, eighteen years, chronic (2½ months). Red blood-cells, 3,840,000; hæmoglobin, 76 per cent.; bleeding time, fourteen minutes; platelets, 5,000. After splenectomy, bleeding time, 2½ minutes; platelets, 130,000. Patient in perfect health. Reported seven months after splenectomy. Cure.

CASE V by Beer,⁷ 1926. Male, thirteen years, chronic (four weeks). Red blood-cells, 3,472,000; hæmoglobin, 67 per cent.; bleeding time, ten minutes; platelets, 20,000. After splenectomy, bleeding time (?); platelets, 550,000. Patient in excellent health. Reported five months after splenectomy. Cure.

CASE VI by Beer,⁷ 1926. Female, twenty-two years, chronic (six months). Red blood-cells, 1,168,000; hæmoglobin, 22 to 33 per cent.; bleeding time, ten minutes; platelets, 2,500. Transfusions before operation. After splenectomy, bleeding time (?), platelets (?). Died three hours after operation. No autopsy. Death.

CASE VII by Falconer and McLachlan,⁸⁸ 1926. Female, ten years, chronic (three months). Red blood-cells, (?); hæmoglobin, (?); bleeding time, prolonged; platelets, occasional. Thrombin injections, calcium lactate, intravenous afenil, transfusions. After splenectomy, bleeding time, (?); platelets, (?). No bleeding after operation. Reported two months after splenectomy. Cure.

CASE VIII by Falconer and McLachlan,⁸⁸ 1926. Female, twenty-eight years, chronic (eight months). Red blood-cells, 800,000; hæmoglobin, (?); bleeding time, eleven to fifteen minutes; platelets, scanty. Transfusions before operation. After splenectomy, bleeding time, four minutes; platelets—no apparent increase found. Clinically cured. Death followed spontaneous delivery of stillborn child two months after operation. Reported two months after splenectomy. Cure (?).

CASE IX by Harris,⁸⁹ 1926. Female, eleven years, chronic (three years). Red blood-cells, 3,880,000 to 3,260,000; hæmoglobin, 85 to 75 per cent.; bleeding time, twenty-five to thirty minutes; platelets, 12,500 to 16,600. Packing, transfusion and tampon

SPLENECTOMY IN PURPURA HEMORRHAGICA

before operation. After splenectomy, bleeding time, two to six minutes; platelets, 595,000 to 504,000. No recurrence. Reported eight months after splenectomy. Cure.

CASE X by Hodges,⁶⁸ 1926. Female, fifteen years, chronic (one year). Red blood-cells, 3,970,000 to 5,000,000; hæmoglobin, 55 to 85 per cent.; bleeding time, twelve minutes; platelets, 40,000 to 16,000. Transfusion before operation. After splenectomy, bleeding time, four minutes; platelets, 198,000 to 1,200,000. Periods reëstablished normally. Reported one year after operation. Cure.

CASE XI by Kerlin,⁷⁷ 1926. Female, fourteen years, chronic (seven years). Red blood-cells, 1,240,000 to 2,730,000; hæmoglobin, 65 to 40 per cent.; bleeding time, five minutes; platelets, 35,000 to 40,000. D and C, radium, transfusions before operation. After splenectomy, bleeding time, four minutes; platelets, 40,000 to 160,000. Patient gaining weight and strength. Reported one year after splenectomy. Cure.

CASE XII by Reilingh,¹¹⁸ 1926. Female, forty-nine years, chronic (2½ years). Red blood-cells, (?); hæmoglobin, (?); bleeding time, (?); platelets, (?). Calcium chloride, peptone before operation. After splenectomy, bleeding time, (?); platelets, 24,000 to 1,017,000. No post-operative hæmorrhages. Reported five months after operation. Cure.

CASE XIII by Crawford and Ogilvie,²⁰ 1927. Female, seven and one-half years, chronic (two years, one month). Red blood-cells, 2,500,000 to 3,400,000; hæmoglobin, 25 per cent.; bleeding time, thirty to twenty minutes; platelets, 7,700 to 3,000. Transfusions, horse serum (intramuscular), tonsillectomy, before operation. After splenectomy, bleeding time, four to seven to six minutes; platelets, 40,000 to 21,000. Patient well six months after operation. Reported six months after splenectomy. Cure.

CASE XIV by Crawford and Ogilvie,²⁰ 1927. Female, seven years, chronic (five months). Red blood-cells, 4,500,000; hæmoglobin, 80 per cent.; bleeding time, twelve minutes; platelets, 22,000. Transfusions before operation. After splenectomy, bleeding time, 0 to two minutes; platelets, 800,000 to 1,500,000 to 200,000. No purpura since operation. Reported four months after splenectomy. Cure.

CASE XV by De Leeuw,²¹ 1927. Sex (?), thirty-six years, chronic (twenty-two years). Red blood-cells, 1,600,000; hæmoglobin, 63 per cent.; bleeding time, eight minutes; platelets, 3,800. Transfusions before operation. After splenectomy, bleeding time, 3½ to 4 minutes; platelets, 190,000. Cure.

CASE XVI by Marin,⁹⁶ 1927. Male, eleven years, chronic (eight years). Red blood-cells, 3,500,000; hæmoglobin, 75 to 40 per cent.; bleeding time, twenty-five to thirty minutes; platelets, 25,000 to 15,000. After splenectomy, bleeding time, 1 to 3½ minutes; platelets, 880,000 to 250,000. Cure.

CASE XVII by Muller,¹⁰⁴ 1927. Female, twenty-six years, chronic (four months). Red blood-cells, (?); hæmoglobin, (?); bleeding time, (?); platelets, 10,000 to 30,000. After splenectomy, bleeding time, (?); platelets, 100,000. Reported two years after splenectomy. Cure.

CASE XVIII by Muller,¹⁰⁴ 1927. Female, twenty-six years, chronic (fifteen years). Red blood-cells, (?); hæmoglobin, (?); bleeding time, (?); platelets, 5,000. After splenectomy, bleeding time, (?); platelets, 160,000. Reported six years after splenectomy. Cure.

CASE XIX by Narog,¹⁰⁰ 1927. Male, eighteen years. Cure.

CASE XX by Schaack,¹²⁰ 1927. Female, nineteen years, chronic (six years). Red blood-cells, 4,000,000 to 4,500,000; hæmoglobin, 40 per cent.; bleeding time, twenty-seven minutes; platelets, few. After splenectomy, bleeding time, (?); platelets, 125,000 to 568,000. Next period normal. Cure.

CASE XXI by Schaak,¹²⁸ 1927. Female, thirty-five years, chronic (twenty years). Red blood-cells, 3,000,000 to 4,000,000; hæmoglobin, 40 to 75 per cent.; bleeding time, prolonged; platelets, 8,000. Gelatinum, ergotin, calcium solutions before operation. After splenectomy, bleeding time, three minutes; platelets, 300,000 to 92,000. Patient well. Reported six months after splenectomy. Cure.

CASE XXII by Schaak,¹² 1927. Female, twenty-eight years, chronic (thirteen years). Red blood-cells, 3,000,000 to 4,500,000; hæmoglobin, 60 to 70 per cent.; bleeding time, twenty to thirty minutes; platelets, 1,000 to 2,000. Protein therapy, X-ray. Eight months in bed. Gelatinum, calcium before splenectomy. After splenectomy, bleeding time, 4 to 4½ minutes; platelets, 115,000 to 400,000. Patient well. Reported two months after splenectomy. Cure.

CASE XXIII by Ceballos and Taubenschlag,¹⁰ 1928. Female, thirty-two years, acute (nine days). Red blood-cells, 2,440,000; hæmoglobin, 34 per cent.; bleeding time, prolonged; platelets, none. Sulpharsenol, lavages, serum, propidon, transfusion before operation. After splenectomy, bleeding time, (?); platelets, normal. Hæmorrhages not repeated after operation. Reported 1½ years after splenectomy. Cure.

CASE XXIV by Emil-Weil and Grégoire,²¹ 1928. Sex, (?), thirty-one years, chronic (nineteen years). Red blood-cells, 1,883,000 to 4,800,000; hæmoglobin, 85 per cent.; bleeding time, four to twenty-nine minutes; platelets, (?). Transfusions, nasal packing before operation. After splenectomy, bleeding time, 1½ to 6 minutes; platelets, 210,000. Patient in good condition. Reported four months after splenectomy. Cure.

CASE XXV by Gosset, Chevalier and Gutmann,⁴⁸ 1928. Female, age, (?), chronic (thirteen years). Red blood-cells, 2,305,000; hæmoglobin, 40 per cent.; bleeding time, sixteen to thirty minutes; platelets, 180,000. X-ray of long bones before operation. After splenectomy, bleeding time, 2½ to 2 minutes; platelets, 264,000 to 237,000. Bleeding stopped first day. Patient has few nose-bleeds when tired. Cure.

CASE XXVI by Green,³¹ 1928. Female, thirty-nine years, chronic (four years). Red blood-cells, 2,000,000 to 4,200,000; hæmoglobin, 48 to 82 per cent.; bleeding time, two minutes; platelets, 70,000 to 500,000. Transfusions and ultra-violet before operation. After splenectomy, bleeding time, two minutes; platelets, 800,000. Epistaxis seven days after operation. Result, unknown.

CASE XXVII by Gregory,⁶⁴ 1928. Male, aged seven, chronic (two years). Red blood-cells, 1,765,000; hæmoglobin, 25 per cent.; bleeding time, fifteen minutes; platelets, 47,700. Transfusions before operation. After splenectomy, bleeding time, 20 to 4½ minutes; platelets, 150,000 to 120,000. Patient had one small epistaxis during convalescence and two since. Reported ten months after splenectomy. Improvement.

CASE XXVIII by Jones, H. C.,⁷⁰ 1928. Female, thirty-three years, chronic (six months). Red blood-cells, 2,150,000; hæmoglobin, 21 per cent.; bleeding time, 23½ to six to eighteen minutes; platelets, 100,000 to 211,000. Transfusions before operation. After splenectomy, bleeding time, five minutes; platelets, 352,000 to 552,000. Patient well. Reported one year after splenectomy. Cure.

CASE XXIX by Kennedy,⁷⁶ 1928. Female, eleven years, chronic (five years). Red blood-cells, (?); hæmoglobin, (?); bleeding time, sixty minutes; platelets, 46,000. After splenectomy, bleeding time, five minutes; platelets, 430,000 to 50,000. Patient had slight epistaxis six weeks after operation. Condition good. Reported four years after splenectomy. Cure.

CASE XXX by Kennedy,⁷⁶ 1928. Female, eleven years, chronic (5½ years). Red blood-cells, (?); hæmoglobin, (?); bleeding time, eleven minutes; platelets, 98,000. After splenectomy, bleeding time, three minutes; platelets, 640,000 to 296,000. Condition excellent. Reported four years after splenectomy. Cure.

CASE XXXI by Kennedy,⁷⁶ 1928. Female, six years, acute (three weeks). Red blood-cells, (?); hæmoglobin, (?); bleeding time, ninety minutes; platelets, 44,000. After splenectomy, bleeding time, three minutes; platelets, 316,000 to 280,000. Condition excellent. Reported three years after splenectomy. Cure.

CASE XXXII by Kennedy,⁷⁶ 1928. Male, ten years, chronic (eight months). Red blood-cells, (?); hæmoglobin, (?); bleeding time, sixty minutes; platelets, 56,000. After splenectomy, bleeding time, (?); platelets, 372,000. Condition excellent. Reported two years after splenectomy. Cure.

SPLENECTOMY IN PURPURA HEMORRHAGICA

CASE XXXIII by Kennedy,⁷⁸ 1928. Male, nine years, chronic (three years). Red blood-cells, (?); hæmoglobin, (?); bleeding time, eighteen minutes; platelets, 36,000. After splenectomy, bleeding time, (?); platelets, (?). Condition excellent. Reported two years after splenectomy. Cure.

CASE XXXIV by Kennedy,⁷⁸ 1928. Male, four and one-half years, chronic (seven weeks). Red blood-cells, (?); hæmoglobin, (?); bleeding time, forty-eight minutes; platelets, 50,000. After splenectomy, bleeding time, (?); platelets, 328,000 to 120,000. No recurrence. Reported six months after splenectomy. Cure.

CASE XXXV by Kennedy,⁷⁸ 1928. Female, eight and one-half years, chronic (four months). Red blood-cells, (?); hæmoglobin, (?); bleeding time, twenty minutes; platelets, 64,000. After splenectomy, bleeding time, two minutes; platelets, 224,000 to 258,000. No recurrence. Reported two years after splenectomy. Cure.

CASE XXXVI by Kennedy,⁷⁸ 1928. Female, seven years, chronic (two years). Red blood-cells, (?); hæmoglobin, (?); bleeding time, twenty-eight minutes; platelets, 144,000. After splenectomy, bleeding time, twenty-eight minutes; platelets, 242,000 to 208,000. Condition excellent. Reported two years after splenectomy. Cure.

CASE XXXVII by Kennedy,⁷⁸ 1928. Female, nine years, chronic (seven and one-half years). Red blood-cells, (?); hæmoglobin, (?); bleeding time, sixty minutes; platelets, 300,000. After splenectomy, bleeding time, 120 minutes; platelets, 352,000 to 272,000. No epistaxis or purpura following operation. Patient menstruates profusely. Reported four years after splenectomy. Cure.

CASE XXXVIII by Kennedy,⁷⁸ 1928. Female, four years, acute (one week). Red blood-cells, (?); hæmoglobin, (?); bleeding time, twenty-six minutes; platelets, 98,000. After operation, bleeding time, thirteen minutes; platelets, 208,000 to 88,000. No improvement following operation. Death followed tonsillectomy two months later. Unimproved.

CASE XXXIX by Lesne, Marquezy and Stieffel,⁸² 1928. Female, twenty-three years, chronic (sixteen years). Red blood-cells, 3,400,000; hæmoglobin, 70 per cent.; bleeding time, seventeen minutes to three hours; platelets, 50,000. Hospitalized many times, radiotherapy, serum, anthema, peptone, calcium chloride, thyroid and ovarian extract. After splenectomy, bleeding time, nine to five to thirty minutes; platelets, 200,000 to 50,000. Purpura one month after operation. One epistaxis requiring packing. Judgment reserved. Reported one year after splenectomy. Improvement.

CASE XL by Merklen and Leriche,¹⁰⁹ 1928. Female, seventeen years, chronic (eight months). Red blood-cells, 1,480,000; hæmoglobin, 26 per cent.; bleeding time, forty minutes; platelets, 26,000 to 28,000. Transfusions, irradiations of spleen, coagulen before operation. After splenectomy, bleeding time, four to twenty-one to seven minutes; platelets, 18,200 to 200,000. No bleeding following operation. Reported six months after splenectomy. Cure.

CASE XLI by Pinkerton,¹¹⁰ 1928. Female, eighteen years, chronic (four months). Red blood-cells, 1,080,000; hæmoglobin, 20 per cent.; bleeding time, thirty minutes; platelets, 18,000. Transfusion, nasal packing, hemostatics before operation. After splenectomy, bleeding time, 2½ minutes; platelets, 80,000 to 20,000. Purpuric spots on ankle twelfth day. Trace of blood from gums fifth and twelfth days. Otherwise uneventful convalescence. Reported four months after splenectomy. Cure.

CASE XLII by Reuben and Claman,¹¹⁹ 1928. Female, three and one-half years, acute (three days). Red blood-cells, 3,200,000 to 2,700,000; hæmoglobin, 73 to 48 per cent.; bleeding time, prolonged; platelets, 55,000 to 10,000. Transfusions before operation. After splenectomy, bleeding time, (?); platelets, 68,000 to 590,000. Patient operated upon for acute mastoiditis following splenectomy and complete healing took one year. Now well in every respect. Reported eighteen months after splenectomy. Cure.

CASE XLIII by Reuben and Claman,¹¹⁹ 1928. Male, six and one-half years, chronic (three months). Red blood-cells, 4,500,000; hæmoglobin, 70 per cent.; bleeding time, fifteen minutes; platelets, 78,000. Transfusions, alpine treatments, milk injections,

adrenalin before operation. After splenectomy, bleeding time, (?); platelets, 385,000 to 487,000. No recurrence. Reported four months after splenectomy. Cure.

CASE XLIV by Reuben and Claman,¹¹⁹ 1928. Female, nine and one-half years, acute (nine days). Red blood-cells, 3,500,000; bleeding time, twenty minutes; platelets, 40,000 to 50,000. "All medical measures," transfusions before splenectomy. After splenectomy, bleeding time, 3½ to 45 to 17 minutes; platelets, 43,000—few. Patient clinically cured but still has thrombopenia, delayed clot retraction, increased bleeding time. Reported three months after splenectomy. Cure.

CASE XLV by Reuben and Claman,¹¹⁹ 1928. Male, seven years, chronic (two years). Red blood-cells, (?); hæmoglobin, (?); bleeding time, seven minutes; platelets, 20,800 to 124,000. Transfusions before operation. After splenectomy, bleeding time, (?); platelets, (?). Purpuric spots after splenectomy; also bleeding from mucous membrane. Improvement.

CASE XLVI by Reuben and Claman,¹¹⁹ 1928. Male, eight years, chronic (four months). Red blood-cells, 3,900,000; hæmoglobin, 68 per cent.; bleeding time, three and one-half minutes; platelets, 60,000. Transfusion and "other treatment" before operation. After splenectomy, bleeding time, (?); platelets, 62,000 to 483,400. Condition excellent. Reported one year after splenectomy. Cure.

CASE XLVII by Rhame,¹²⁰ 1928. Female, seventeen years, chronic (three months). Red blood-cells, 4,272,000; hæmoglobin, 85 to 86 per cent.; bleeding time, twenty-five to eight minutes; platelets, 78,000 to 149,000. Horse serum, nasal packing, calcium chloride, transfusion before operation. After splenectomy, bleeding time, three minutes; platelets, 220,000 to 374,000. Slight bleeding from uterus checked on fourth day. Patient in excellent health. Reported three months after splenectomy. Cure.

CASE XLVIII by Schiassi,¹²¹ 1928. Female, forty years. Other data (?). After splenectomy, no hemorrhagic symptoms. Reported four months after splenectomy. Cure.

CASE XLIX by Stewart,¹²¹ 1928. Female, three and one-half years, chronic (one year). Red blood-cells, 3,552,000 to 4,530,000; hæmoglobin, 61 to 52 per cent.; bleeding time, seven minutes; platelets, 50,000 to 22,000. Calcium lactate, ultra-violet radiation, transfusions before operation. After splenectomy, bleeding time, one and one-half minutes; platelets, 40,000 to 240,000. No recurrence. Reported three and one-half months after splenectomy. Cure.

CASE L by Stewart,¹²¹ 1928. Female, six and one-half years, chronic (sixteen months). Red blood-cells, 2,184,000 to 1,345,000; hæmoglobin, 70 to 22 per cent.; bleeding time, eight to fourteen to 3½ minutes; platelets, 300,000 to 84,000 to 235,000 to 115,000. Transfusion, liver diet, ultra-violet before operation. After splenectomy, bleeding time, five minutes; platelets, 100,000 to 380,000 to 290,000. Reported five and one-half months after splenectomy. Cure.

CASE LI by Anschütz,² 1928. Female, forty-two years, acute (two days). Red blood-cells, 4,200,000 to 2,460,000; hæmoglobin, 85 to 45 per cent.; bleeding time, prolonged; platelets, 32,000. Transfusion before operation. After splenectomy, bleeding time, two hours; platelets, 320,000; platelets at one year are 319,000. Reported one year after splenectomy. Cure.

CASE LII by Bykowa,¹² 1928. Male, thirty-one years, acute (four weeks). Red blood-cells, 4,800,000; hæmoglobin, 97 per cent.; bleeding time, (?); platelets, 64,200. After splenectomy, bleeding time, (?); platelets, (?). Death first post-operative day.

CASE LIII by Raine, Yates, and Davis,¹²⁰ 1928. Female, fifteen years, chronic (one month). Red blood-cells, 1,250,000 to 3,560,000; hæmoglobin, 44 per cent.; bleeding time, (?); platelets, few—165,000. Transfusions, X-ray before operation. After splenectomy, bleeding time, (?); platelets, 87,500 to 375,000. No further bleeding. Reported six months after splenectomy. Cure.

CASE LIV by Schaack,¹²⁴ 1928. Male, twenty-seven years, chronic. Red blood-cells, 3,220,000; hæmoglobin, 82 per cent.; bleeding time, two minutes; platelets, 59,000. After

SPLENECTOMY IN PURPURA HEMORRHAGICA

splenectomy, bleeding time, (?); platelets, 274,000 to 466,000. No recurrence. Reported one year after splenectomy. Cure.

CASE LV by Schaack,¹²⁴ 1928. Female, forty years, acute (five weeks). Red blood-cells, 1,200,000; hæmoglobin, 20 per cent.; bleeding time, twenty-nine minutes; platelets, 25,000. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, 100,000 to 350,000. Clinically cured. Death from pneumonia four months. Cure.

CASE LVI by Woenckhaus,¹²⁹ 1928. Male, thirty years, chronic (two years). Red blood-cells, 5,060,000; hæmoglobin, 74 per cent.; bleeding time, four to five minutes; platelets, 44,000. Serum, X-ray before operation. After splenectomy, bleeding time, (?); platelets, 156,000 to 230,000. Bleeding continued in spite of platelet-count increase, bleeding time and retractility. Reported three months after splenectomy. Improvement.

CASE LVII by Ceballos and Taubenschlag,¹³ 1929. Female, chronic (seven months). Red blood-cells, (?); hæmoglobin, (?); bleeding time, prolonged; platelets, 118,000. Citrated blood into left radial artery second and third days before operation. After splenectomy, bleeding time, (?); platelets, 142,000 to 164,720. No blood lost following operation. Reported six months after splenectomy. Cure.

CASE LVIII by Ceballos and Taubenschlag,¹³ 1929. Female, thirty-two years, chronic (five months). Red blood-cells, 1,850,000; hæmoglobin, (?); bleeding time, twenty-nine minutes; platelets, scanty. After splenectomy, bleeding time, (?); platelets, almost normal. Cure.

CASE LIX by Ceballos and Taubenschlag,¹³ 1929. Female, twenty-five years, chronic (four months). Red blood-cells, 4,700,000 to 2,000,000; hæmoglobin, 85 per cent.; bleeding time, (?); platelets, 50,000 to 8,000. Calcium chloride, glucose, coagulen, transfusions, bed inclined before splenectomy. After splenectomy, bleeding time, (?); platelets, 214,000 to 221,000. Patient was prepared before operation so that hæmorrhages had stopped. Cure.

CASE LX by Ceballos and Taubenschlag,¹³ 1929. Female, twenty-five years, chronic (two years). Red blood-cells, 3,000,000; hæmoglobin, (?); bleeding time, eight minutes; platelets, 2,346. Bicyanide of mercury before operation. After splenectomy, bleeding time, (?); platelets, 179,000 to 185,000. Cure.

CASE LXI by Frank,⁴² 1929. Male, five years, chronic (two months). Red blood-cells, 1,200,000 to 2,000,000; hæmoglobin, 60 per cent.; bleeding time, sixteen minutes; platelets, 37,000. Transfusions before operation. After splenectomy, bleeding time, (?); platelets, 210,000. No bleeding after operation. Reported five months after splenectomy. Cure.

CASE LXII by Killins,⁷⁹ 1929. Male, twenty-four years, acute. Red blood-cells, 1,200,000 to 3,400,000; hæmoglobin, 85 to 70 per cent.; bleeding time, thirty minutes; platelets, 18,000 to 4,000 to 27,000. Transfusion before operation. After splenectomy, bleeding time, normal; platelets, 400,000 to 380,000 to 165,000. Patient in perfect health. Reported three months after splenectomy. Cure.

CASE LXIII by Kogen and Genkin,⁸⁰ 1929. Male, twenty years, chronic (eight years). Red blood-cells, 5,660,000 to 4,590,000; hæmoglobin, 93 to 60 per cent.; bleeding time, ten minutes; platelets, 2,000 to 15,000 to 9,300. Calcium chloride, autohemotherapy, horse serum, neosalvarsan, mercury before operation. After splenectomy, bleeding time, 2½ minutes; platelets, 128,000 to 874,000 to 154,000. Patient well. Reported 13½ months after splenectomy. Cure.

CASE LXIV by Koster,⁸¹ 1929. Male, twelve years, six weeks' duration. Red blood-cells, 1,520,000; hæmoglobin, 20 per cent.; bleeding time, twenty minutes; platelets, 68,000. Transfusion before operation. After splenectomy, bleeding time, twelve minutes; platelets, 78,000 to 120,000. Death three months following operation from myelogenous leukaemia. Death.

CASE LXV by Koster,⁸¹ 1929. Female, seven years, chronic (one year). Red blood-cells, 3,400,000; hæmoglobin, 48 per cent.; bleeding time, forty-eight minutes; platelets, 15,700. Transfusions before operation. After splenectomy, bleeding time, twelve

minutes; platelets, 190,000. No recurrence. Reported fifteen months after splenectomy. Cure.

CASE LXVI by Koster,⁸¹ 1929. Female, twenty years, chronic (six months). Red blood-cells, 1,688,000; hæmoglobin, 23 per cent.; bleeding time, twenty-three minutes; platelets, 30,000 to 20,000. Transfusion after operation. After splenectomy, bleeding time, twenty-six minutes, platelets, 350,000. Result unknown.

CASE LXVII by Leriche and Horrenberger,⁸¹ 1929. Male, eleven and one-half years, chronic (six months). Red blood-cells, 5,100,000 to 4,610,000; hæmoglobin, 55 per cent.; bleeding time, twenty-three minutes to four hours to 14½ minutes; platelets, 86,000 to 120,000 to 169,000. Calcium chloride, transfusions, X-ray of spleen, nose, buttocks, both femurs, coagulen, anthema before operation. After splenectomy, bleeding time, twenty-seven minutes; platelets, 68,000 to 400,000 to 600,000. Patient in perfect health. Reported 8½ months after operation. Cure.

CASE LXVIII by Litchfield,⁸⁶ 1929. Female, six years, acute (two days). Red blood-cells, 2,260,000; hæmoglobin, 50 to 45 per cent.; bleeding time, fourteen minutes; platelets, 30,000 to 80,000 to 25,000. Intramuscular blood injections, transfusions before operation. After splenectomy, bleeding time, (?); platelets, 250,000 to 525,000. Cure.

CASE LXIX by Plumier-Clermont and Lambrecht,¹³¹ 1929. Female, four and one-half years, chronic (six months). Red blood-cells, 5,000,000; hæmoglobin, 80 to 40 per cent.; bleeding time, ninety-three minutes; platelets, (?); ten cubic centimetres propeptone, 5 per cent. intramuscular weekly hemoplastin injections before operation. After splenectomy, bleeding time, 5½ to 3½ minutes; platelets, 800 to 600,000 to 615,000. Reported two months after operation. Improvement.

CASE LXX by Quénu and Stoianovitch,¹¹⁸ 1929. Immediate improvement following operation with death eleven months post-operative. Recurrence.

CASE LXXI by Schaak,¹³⁰ 1929. Female, twenty-five years, chronic (nine years). Red blood-cells, 2,300,000; hæmoglobin, 80 per cent.; bleeding time, twenty-four minutes; platelets, 8,000. Röntgen-rays and other treatments before operation. After splenectomy, bleeding time, (?); platelets, 500,000. Patient well. Cure.

CASE LXXII by Abrahamsen and Meulengracht,¹ 1930. Female, twenty-four years, chronic (two years). Red blood-cells, 1,800,000 to 4,800,000; hæmoglobin, 28 to 80 per cent.; bleeding time, two hours, prolonged; platelets, 5,000 to 150,000. Transfusions before operation. After splenectomy, bleeding time, two to three minutes; platelets, 90,000 to 603,000 to 17,200. Patient has occasional bleedings. Reported twenty months after splenectomy. Improvement.

CASE LXXIII by Abrahamsen and Meulengracht,¹ 1930. Female, twenty-two years, chronic (eight years). Red blood-cells, 1,700,000; hæmoglobin, 57 to 30 per cent.; bleeding time, fifteen minutes; platelets, 1,000 to 5,000. Serum, pelvic operation before splenectomy. After splenectomy, bleeding time, five to thirty minutes; platelets, 17,000 to 57,000 to 33,000. Petechia, bleeding on slight trauma. Reported fourteen months after splenectomy. Improvement.

CASE LXXIV by Graham,⁴⁹ 1930. Female, sixteen years, acute (two days). Red blood-cells, 2,400,000 to 3,136,000; hæmoglobin, 25 to 48 to 20 to 27 per cent.; bleeding time, sixteen minutes; platelets, 31,000 to 40,000 to 136,000. Ergot, transfusions, dilatation, curettage, packing, thromboplastin before splenectomy. After splenectomy, bleeding time, 2½ to 1½ minutes; platelets, 310,000 to 208,000 to 536,000. Vaginal bleeding until fourth post-operative day. Reported five months after splenectomy. Cure.

CASE LXXV by Kerlin,⁷⁸ 1930. Female, fourteen years, chronic (eight years). Red blood-cells, 2,060,000 to 1,780,000; hæmoglobin, 60 to 40 per cent.; bleeding time, six minutes; platelets, 49,000 to 40,000. After splenectomy, bleeding time, (?); platelets, 150,000 to 148,000. Condition good. Reported four years after splenectomy. Cure.

CASE LXXVI by Kerlin,⁷⁸ 1930. Female, fifteen years, chronic (eleven years). Red blood-cells, 2,120,000 to 1,856,000; hæmoglobin, 65 to 40 per cent.; bleeding time, 10½ minutes; platelets, 140,000 to 82,000. After splenectomy, bleeding time, eight min-

SPLENECTOMY IN PURPURA HEMORRHAGICA

utes; platelets, 136,000 to 260,000. Patient in excellent health. Reported three years after splenectomy. Cure.

CASE LXXVII by Kerlin,⁷⁸ 1930. Male, ten years, chronic (seven years). Red blood-cells, 2,720,000; hæmoglobin, 75 per cent.; bleeding time, seven minutes; platelets, 48,000. Transfusions before splenectomy. After splenectomy, bleeding time, sixty minutes; platelets, (?). Death three hours after operation.

CASE LXXVIII by Kerlin,⁷⁸ 1930. Female, eighteen years, chronic (two years). Red blood-cells, 1,440,000 to 3,448,000; hæmoglobin, 20 to 45 per cent.; bleeding time, thirty to six minutes; platelets, 270,000 to 370,000 to 160,000. Eight months before operation transfusion, calcium chloride, gelatine, ultra-violet. After splenectomy, bleeding time, 3½ minutes; platelets, 240,000. Condition good. Reported two and one-half months after splenectomy. Cure.

CASE LXXIX by Marsh,⁹⁷ 1930. Male, forty-five years, acute (one week). Red blood-cells, 3,300,000 to 4,600,000; hæmoglobin, 58 per cent.; bleeding time, thirty minutes; platelets, 95,000 to 120,000. Transfusions before splenectomy. After splenectomy, bleeding time, 9 to 2½ minutes; platelets, 135,000 to 180,000. No recurrence. Cure.

CASE LXXX by Sakai,¹²² 1930. Cure.

CASE LXXXI by Washburn,¹²⁰ 1930. Female, fifteen years, chronic (seven years). Red blood-cells, 2,500,000; hæmoglobin, 25 per cent.; bleeding time, 64½ minutes; platelets, 112,000. Transfusions before operation. After splenectomy, bleeding time, ten minutes; platelets, 81,000 to 4,000. Oozing from gums and wound for four days post-operative. Profuse menstruation seventh day, controlled by transfusions. Continuous slight oozing from gums. Slight improvement. Reported four years after splenectomy. Improvement.

CASE LXXXII by Washburn,¹²⁰ 1930. Male, four and one-half years, chronic (nine months). Red blood-cells, 4,800,000; hæmoglobin, 75 per cent.; bleeding time, forty-five minutes; platelets, 28,000 to 4,000 to 13,000. Transfusions before operation. After splenectomy, bleeding time, (?); platelets, 1,175,000 to 224,000. No bleeding following operation. Reported eighteen months after splenectomy. Cure.

CASE LXXXIII by Washburn,¹²⁰ 1930. Male, four years, chronic (three months). Red blood-cells, 3,600,000; hæmoglobin, 80 per cent.; bleeding time, thirty minutes; platelets, 32,000. Transfusions before operation. After splenectomy, bleeding time, (?); platelets, 2,163,000 to 480,000. Result good. Reported five months after splenectomy. Cure.

CASE LXXXIV by Bloomfield,¹⁰ 1931. Male, thirty-four years, chronic (six months). Red blood-cells, 2,550,000; hæmoglobin, 46 per cent.; bleeding time prolonged; platelets, 9,000. Transfusions, iron, liver, calcium lactate, X-ray before operation. After splenectomy, bleeding time prolonged, normal; platelets, 44,000 to 340,000 to 20,000. No spleen found. Patient was discharged clinically well two months post-operative. Readmitted six weeks later. Death 3½ months post-operative from cerebral hæmorrhage. Death.

CASE LXXXV by deSanctis and Allen,²⁶ 1931. Male, eight years, acute (two weeks). Red blood-cells, 3,900,000 to 4,200,000 to 3,900,000; hæmoglobin, 68 to 81 to 68 per cent.; bleeding time, 3½ to 6½ minutes; platelets, 60,000 to 33,600 to 14,000. Fluids, stimulants, nasal packing, fibrinogen, thromboplastin, calcium chloride, transfusion before operation. After splenectomy, bleeding time, (?); platelets, 62,000 to 430,000 to 280,000. No recurrence. Reported 4½ years after operation. Cure.

CASE LXXXVI by deSanctis and Allen,²⁶ 1931. Male, ten years, chronic (two years). Red blood-cells, 2,400,000; hæmoglobin, 50 per cent.; bleeding time, seven minutes; platelets, 31,000. Transfusions before operation. After splenectomy, bleeding time, (?); platelets, 93,500 to 180,000. Patient well. Cure.

CASE LXXXVII by deSanctis and Allen,²⁶ 1931. Male, five and one-quarter years, chronic (several months). Red blood-cells, 550,000; hæmoglobin, 28 per cent.; bleeding time, four minutes; platelets, 21,700 to 12,000. Packing, transfusion before operation.

After splenectomy, bleeding time, $3\frac{1}{2}$ minutes; platelets, 85,000 to 302,000 to 244,700. Patient weathered lobar pneumonia, myringotomy, mastoidectomy. Repeatedly readmitted for epistaxis which gradually becomes less. Condition good. Reported two years after splenectomy. Improvement.

CASE LXXXVIII by Donovan,²⁸ 1931. Male, fifty years, acute (three days). Red blood-cells, 3,900,000; hæmoglobin, 69 per cent.; bleeding time, normal; platelets, 80,000 to 25,000. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, 23,000 to 560,000 to 290,000. No post-operative bleeding. Reported thirteen days after operation. Cure.

CASE LXXXIX by Kretschmar,²⁹ 1931. Female, thirty-one years, chronic (seven years). Red blood-cells, (?); hæmoglobin, 15 per cent.; bleeding time, twenty minutes; platelets, 30,000. After splenectomy, bleeding time, prolonged; platelets, 500,000. Clinically cured following operation. Recurrence and cure following transfusion. Reported four years after splenectomy. Cure.

CASE XC by Le Marquand and Mills,³⁰ 1931. Female, fifty-two years, acute (one week). Red blood-cells, 4,300,000; hæmoglobin, 80 to 90 per cent.; bleeding time, (?); platelets, 26,000 to 120,000. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, 400,000. Reported six months after splenectomy. Cure.

CASE XCI by McLean, Kreidel and Caffey,³⁰ 1931. Acute (one month). Red blood-cells, 2,500,000; hæmoglobin, 40 per cent.; bleeding time, sixty hours; platelets, 32,000 to 56,000. Transfusion before splenectomy. After splenectomy, bleeding time, (?); platelets, (?). Ligation of aberrant gastric vein. Death.

CASE XCII by McLean, Kreidel and Caffey,³⁰ 1931. Chronic (thirteen months). Red blood-cells, 1,900,000; hæmoglobin, 40 per cent.; bleeding time, ten minutes; platelets, 10,000 to 20,000. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, (?). Bleeding from ninth to twenty-fifth days and death twenty-sixth day. Death.

CASE XCIII by McLean, Kreidel and Caffey,³⁰ 1931. Acute (forty-eight hours). Red blood-cells, 2,800,000; hæmoglobin, 60 per cent.; bleeding time, fifteen minutes; platelets, 20,000 to 22,000. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, 440,000 to 600,000. Reported two months after splenectomy. Cure.

CASE XCIV by McLean, Kreidel and Caffey,³⁰ 1931. Chronic (two years). Bleeding time, fifteen minutes; platelets, 10,000 to 16,000. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, 640,000 to 2,200,000 to 824,000. Cure permanent. Reported fourteen months after splenectomy. Cure.

CASE XCV by McLean, Kreidel and Caffey,³⁰ 1931. Acute (two weeks). Red blood-cells, 2,700,000 hæmoglobin, 40 per cent.; bleeding time, twenty-four minutes; platelets, 32,000 to 17,000. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, (?). Complete hemostasis at operation, death following. Death.

CASE XCVI by McLean, Kreidel and Caffey,³⁰ 1931. Acute (forty-eight hours). Red blood-cells, 3,300,000; hæmoglobin, 40 per cent.; bleeding time, $6\frac{1}{2}$ hours; platelets, 36,000 to 56,000. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, 328,000 to 1,176,000 to 448,000. Rapid permanent recovery. Reported four years after splenectomy. Cure.

CASE XCVII by Orloff,¹⁰⁷ 1931. Cure.

CASE XCVIII by Portis,¹¹³ 1931. Male, four and one-half years, chronic (five weeks). Red blood-cells, 1,800,000 to 3,200,000 to 2,400,000; hæmoglobin, 30 to 45 to 40 per cent.; bleeding time, $8\frac{1}{2}$ minutes; platelets, 34,000 to 180,000 to 150,000. Transfusions before operation. After splenectomy, bleeding time, four minutes; platelets, 100,000 to 190,000 to 250,000. No recurrence except one severe nose-bleed five months post-operative. Reported six months after operation. Improvement.

CASE XCIX by Proctor,¹¹³ 1931. Female, forty years, chronic (twenty-five years). Red blood-cells, 1,000,000 to 4,000,000; hæmoglobin, 10 to 45 to 55 per cent.; bleeding time, eight to five to seven minutes; platelets, not counted. Transfusions, radium before

SPLENECTOMY IN PURPURA HEMORRHAGICA

operation. After splenectomy, bleeding time eighteen to $1\frac{1}{2}$ to four minutes; platelets, 350,000 to 750,000 to 330,000 to 120,000. Condition good. Reported five months after splenectomy. Cure.

CASE C by Rankin and Anderson,¹¹⁷ 1931. Male, four years, chronic (one year). Red blood-cells, 3,930,000 to 4,260,000; hæmoglobin, 53 per cent.; bleeding time, sixty to forty minutes; platelets, 30,000 to 40,000, none found. After splenectomy, bleeding time, twenty-five to ten to twenty minutes; platelets, 68,000 to 24,000 to 90,000. Slight nose bleeding until thirteenth day after operation. None since. Reported one month, twenty-three days after splenectomy. Cure.

CASE CI by Smith,⁹⁰ 1931. Child, acute (five weeks). Red blood-cells, (?); hæmoglobin, 35 per cent.; bleeding time, (?); platelets, 80,000 to 20,000. Transfusions before operation. After splenectomy, bleeding time, (?); platelets, 157,000 to 300,000. No further bleeding. Reported six weeks after splenectomy. Cure.

CASE CII by Wilkie,¹¹⁷ 1931. Female, fourteen years, chronic (since infancy). Red blood-cells, 4,600,000; hæmoglobin, 50 per cent.; bleeding time, fourteen minutes; platelets, 18,000. Transfusions before operation. After splenectomy, bleeding time, $4\frac{1}{2}$ minutes; platelets, 150,000 to 230,000 to 190,000. No recurrence. Reported two years after splenectomy. Cure.

CASE CIII by Zondek,¹⁰⁰ 1931. Female, thirty-two years, chronic (fifteen years). Red blood-cells, 4,000,000 to 5,000,000; hæmoglobin, 62 to 73 per cent.; bleeding time up to twenty-three minutes; platelets, 36,000 to 6,000. Transfusions before splenectomy. After splenectomy, clinically well for $4\frac{1}{2}$ years. Sudden recurrence at that time. Recurrence.

CASE CIV by Eliason and Ferguson, 1932. Male, twenty years, chronic (10 years). Red blood-cells, 3,300,000; hæmoglobin, 56 per cent.; bleeding time, $2\frac{1}{2}$ minutes; platelets, few—16,000. Thromboplastin, ceanothyn, transfusion, calcium lactate, antivenin before operation. After splenectomy, bleeding time, $2\frac{1}{2}$ minutes; platelets, 9,200 to 48,000 to 22,000. Continued bleeding for six weeks after operation. None two weeks later. Reported fifteen months after splenectomy. Cure.

CASE CV by Eliason and Ferguson, 1932. Male, seven years, chronic (three years). Red blood-cells, 4,700,000 to 4,490,000; hæmoglobin, 80 per cent.; bleeding time, $19\frac{3}{4}$ to 3 minutes; platelets, 250,000 to 160,000 to 140,000. On readmission following operation: Transfusion ultra-violet, calcium gluconate. After splenectomy, bleeding time, $2\frac{1}{2}$ to 5 to $2\frac{1}{2}$ minutes; platelets, 210,000 to 130,000 to 140,000. Readmitted seventh post-operative month because of purpuric spots and bleeding from gums. Discharged in six weeks. Reported twenty-two months after splenectomy. Cure.

CASE CVI by Eliason and Ferguson, 1932. Male, two and one-half years, acute (eight days). Red blood-cells, 4,180,000; hæmoglobin, 75 to 100 per cent.; bleeding time, one hour; platelets, 2,500 to 28,800 to 12,800. Transfusion before operation. After splenectomy, bleeding time, (?); platelets, 233,000 to 896,000 to 186,000. Excellent health. Reported seven months after operation. Cure.

CASE CVII by Eliason and Ferguson, 1932. Female, thirty-three years; chronic (three and one-half years). Red blood-cells, 2,040,000 to 1,490,000 to 2,380,000; hæmoglobin, 30 to 40 per cent.; bleeding time, prolonged; platelets, 40,000 to 320,000 to 80,000. Transfusion, antivenin, thromboplastin, calcium lactate before operation. After splenectomy, bleeding time, five to three to one minute; platelets, 210,000 to 350,000. Excellent result. Reported one year after operation. Cure.

CASE CVIII by Eliason and Ferguson, 1932. Female, twelve years, acute (two months). Red blood-cells, 1,800,000 to 2,170,000; hæmoglobin, 28 per cent.; bleeding time, thirteen minutes; platelets, 40,000—two few to count. Nasal packing, X-ray over spleen, thromboplastin, transfusions before operation. After splenectomy, bleeding time, (?); platelets, 160,000 to 125,000 to 160,000 to 70,000 to 230,000 to 100,000. Bleeding from nose third post-operative day, probably due to picking of clots. Reported two years, three months after splenectomy. Cure.

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THE TUMORS OF THE STERNUM

REPORT OF REMOVAL OF A LARGE MEDIASTINAL STERNAL CHONDROMYXOMA

By GEORGE J. HEUER, M.D.

OF CINCINNATI, OHIO

THE intrathoracic chondromas and chondromyxomas include a group of tumors arising from the costal cartilages, sternum, costovertebral articulations and spine (intervertebral discs) which encroach upon the intrathoracic space and mediastinum. Pathologically, they comprise two kinds of tumors; those which are solid and made up of cartilage (chondromas), and those which are partly solid (cartilage) and partly cystic—the cystic portion consisting of a ropy, sticky, clear or opalescent fluid or a gelatinous material. Whether these represent two different varieties of cartilaginous tumors or whether the cystic variety called chondromyxoma represents a degeneration form of chondroma is a question I leave for the present outside of this discussion. From the viewpoint of surgery they have the characteristics in common that they are circumscribed, encapsulated tumors which in their growth crowd the thoracic or mediastinal structures to one side, do not as a rule invade them, and rarely become firmly adherent to them. Were it not, then, for the size which they have frequently attained, when patients harboring them present themselves for diagnosis and treatment, their surgical removal should be comparatively simple.

These tumors are not common. In a series of 213 cases of tumor of the ribs and sternum (the collected cases of Parham, Lund and Hedblom) chondromas, chiefly of the costal cartilages, occurred in forty. Of 205 tumors of the ribs and sternum which I personally studied several years ago, 164 (80 per cent.) were tumors of the ribs, thirty-two (15 per cent.) were tumors of the sternum and the remainder (five) scattered. Of the thirty-two sternal tumors studied, twenty were sarcomas; two, chondromas; three, fibromas; two, carcinomas, and one each a gumma and chronic inflammation. It is apparent from these studies that the chondromas and chondromyxomas of the costal cartilages are infrequent and those of the spine and the costovertebral articulations quite rare tumors; suppositions which are borne out by the fact that in a growing series of intrathoracic new growths, I have seen but two examples.

The first is a large intrathoracic chondromyxoma occupying the upper half of the right thoracic cavity and arising presumably from the costovertebral articulations of the fourth and fifth ribs. The case was seen and operated upon in November, 1920, and was reported in the *ANNALS OF SURGERY* in 1924. The second, seen and operated upon within the past year, is a large mediastinal chondromyxoma arising from the sternum and forms the basis of this report. The protocol follows:

THE TUMORS OF THE STERNUM

Miss A. Z., aged fifty-six years, was admitted to the Cincinnati General Hospital June 1, 1931, complaining of pain in the chest and shortness of breath. Her family history is unimportant. She, herself, was well until 1904, when she had what was said to be an attack of pleurisy. Shortly thereafter she noticed a small, hard tumor mass upon the sternum just to the right of the midsternal line. This slowly grew in size and with its growth there occurred, periodically, paroxysms of sharp pain in the right thorax, sometimes extending into the left thorax beneath the left breast. These symptoms continued without much change for fourteen or fifteen years when the tumor rather suddenly began to grow more rapidly in size. She consulted a surgeon (she was then living in Switzerland) who in 1920 removed the tumor and told her it was a harmless growth of cartilage. She was relieved of her pain and apparently was well. On October 28, 1924, she consulted me for an attack of acute upper abdominal pain and a diagnosis of acute cholecystitis was made. I operated upon her at once and removed an acutely inflamed, greatly distended gall-bladder associated with a stone impacted in the cystic duct. She made an uneventful recovery. At this time I learned of the previous operation for chondroma of the sternum and made a careful examination of her chest. There was a curved scar over the lower portion of the sternum about which the sternum was normal on inspection and palpation. The thorax was negative on examination. There was absolutely no external evidence of recurrence at this time and she was quite free from pain. Unfortunately, however, an X-ray of her thorax was not made.

The patient was again well until November of 1929, when she had a recurrence of the "pleurisy" and soon after noticed a recurrence of the tumor. The paroxysms of pain previously complained of became increasingly severe and more frequent. By 1930 the pain was more or less constant with now and then an agonizing, hot, burning pain through her chest. Drugs at first relieved the pain but more recently such huge doses became necessary that she has been in a somnolent condition a good part of the time. X-rays of her chest were made in 1929, 1930, and 1931 and all show a large mediastinal shadow; but a diagnosis was not positively made. Some time before coming to the Cincinnati General Hospital she had some dyspnoea, especially on exertion, and noted some fullness of the vessels of her neck. On her admission to the hospital she was only eight pounds under her previous best weight.

Examination.—The patient's general physical condition is good. There is no dyspnoea or cyanosis while lying quietly in bed. Her color is good. There is a slight ptosis of the left upper lid but no other evidences of involvement of the sympathetic. The patient is alert and coöperative.

The general physical examination is negative excepting for the thorax. Over the upper part of the thorax anteriorly there is a slight but definite enlargement of the superficial veins, the size of which is accentuated by straining and coughing. Projecting from the anterior surface of the sternum is a visible swelling which is flat and which shades imperceptibly into the surrounding bone. It has no definite outlines; approximately it is 6 by 6.5 centimetres in diameter. The swelling is hard and elastic and lies under the scar of the operation performed in 1920. Palpation of it and percussion about it is painful. Expansion of the thorax is good. Percussion and auscultation over the lungs are quite negative. There is definite dullness behind and to either side of the sternum. The cardiac dullness evidently is displaced to the left. The heart sounds are clear.

The blood failed to show anything remarkable. There is a slight anaemia. The urine was negative on several examinations. The Wassermann reaction is negative.

The six series of X-ray films made between December 2, 1929, and June 1, 1931, all show a large mediastinal shadow and displacement of the heart to the left (Fig. 1). Careful comparison of the various films fails to show any appreciable increase in the size of the shadow. In the plates from 1930 on, there appears a small circular shadow in the left costophrenic angle (Fig. 1 M) which was thought to be a possible metastasis

in the lung (This has since been closely followed and films made May 1, 1932, show that it has increased in size. When first observed it measured on the film 1.5 centimetres in diameter; at the present time, two years later, it measures 2.5 centimetres to 3 centimetres in diameter.)

A diagnosis of mediastinal chondroma arising from the sternum was made. It seemed doubtful in view of the large size of the tumor that surgical removal could be successful; yet because of the severity of the pain, an exploration with an attempt at removal seemed justified. The patient readily agreed to such an operation.

Operation was performed June 2, 1931, under positive-pressure gas-oxygen-ether anaesthesia. Since the larger part of the tumor lay on the right side, a curved incision forming a flap was made about three inches from the midsternal line. The skin and subcutaneous tissues were reflected to the right, exposing the pectoral muscle. This was dissected off from the sternum and ribs so as to preserve all muscle possible with

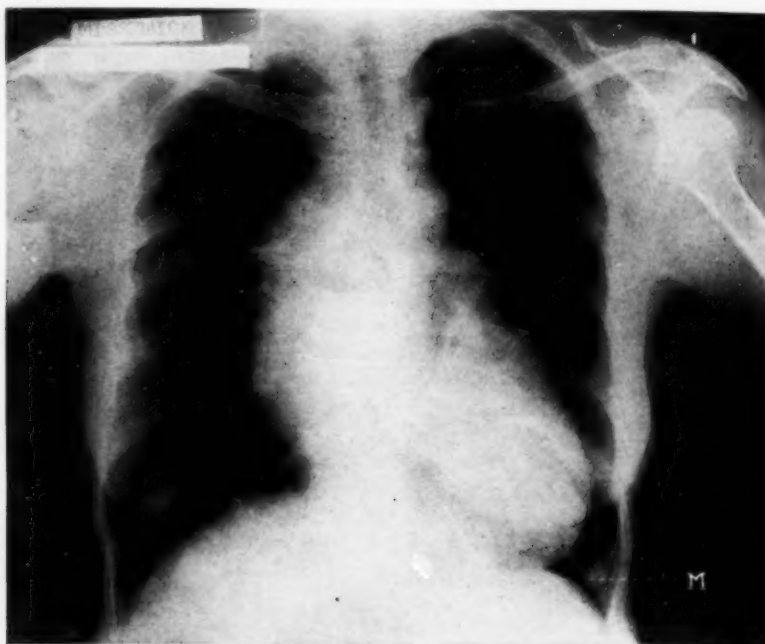


FIG. 1.—X-ray taken before operation. The large mediastinal tumor has crowded the heart to the left. The supposed metastasis in the lung is indicated by "M."

the exception of that portion of it which overlay the external tumor. The muscle being reflected from the costal cartilages, these were freed and divided with a rongeur well to the right of the border of the tumor. The cartilages of the seventh, sixth, fifth, fourth and third ribs were thus divided. An attempt was then made to strip the underlying pleura, but it at once became evident that this was fused with the tumor mass. The pleura therefore was deliberately opened throughout the extent of the wound. The anaesthetist was able to distend the right lung at will so that we proceeded without anxiety.

The right border of the mediastinal tumor was immediately brought into view. The tumor was so large that we were doubtful whether it was wise to attempt its removal. The lower border of the tumor extended downward to the point of attachment of the diaphragm to the xiphoid. Above there was a prolongation of the tumor which extended up to the suprasternal notch. However, it became apparent almost immediately

THE TUMORS OF THE STERNUM

that there were no firm adhesions between the tumor and the surrounding structures, and I proceeded gingerly to free the right lateral border from the adjacent lung. This proved not to be difficult, and in a very short time I had exposed the right side of the tumor throughout its entire length. I continued freeing the tumor upwards and downwards until I had quite encircled both its lower and upper poles. I inserted my hand deeply into the chest and found that I could surround the posterior or dorsal border of the tumor which extended quite to the spine. Very carefully, I swept my hand around the tumor until I came to the left lateral border of the growth, and here I found it lying adjacent to the heart and great vessels. Very fortunately, here also there were no dense adhesions between the tumor and the surrounding structures, and in a very short time I had swept my hand completely around the tumor so that my hand came in contact with the chest wall beyond its left lateral border.

Having gone this far I next continued the resection of the sternum around to the left. This procedure was performed in the same way as on the right side; that is, the pectoral muscle was stripped from the chest wall and the costal cartilages exposed. I then cut across each costal cartilage with a rongeur so that eventually I had surrounded the entire tumor, giving it a wide berth in all directions. The tumor was then removed completely and with the lower two-thirds of the sternum.

Throughout the procedure there was no hæmorrhage whatsoever. There was left the most astonishing opening into the chest I have ever seen. Both lungs lay exposed in the wound, as did the heart and great vessels. Fortunately, although the right pleura was opened widely, the left was not, and the anæsthetist had the situation in perfect control. The right pleural cavity was dried by suction and there remained the closure of the wound. The pectoral muscle on either side was brought to the mid-line and sutured with interrupted sutures of silk. In this procedure the right breast was dislocated mesially and helped very much to fill the cavity. Another layer of sutures was placed in the subcutaneous tissues and the skin was then closed with interrupted fine silk. Just at the end of the procedure, a trochar was introduced into the right thorax and the air aspirated.

At the completion of the closure the patient was in very good condition. There was no cyanosis. The pulse was under 100. What seemed to be a disturbing thing was the remarkable suction inward of the wound on inspiration. This, it seemed to me, might markedly interfere with respiration, defeating the inspiratory act. I therefore made a breast plate of rigid cardboard and fastened it air-tightly over the front of the chest with broad strips of adhesive. Whether this really had anything to do with maintaining proper respiration is doubtful. The respiration remained at all times good and was equally good two days later when the cardboard was removed.

Post-operative notes.—One cannot imagine a smoother post-operative course. The pain immediately disappeared and the patient even in the first days of convalescence was far more comfortable than before the operation. There was at no time any dyspnoea and her color was always good. The wound healed *per primam*. Repeated X-rays taken with a movable unit failed to show any accumulation of fluid in either half of the thorax. There was, for the first week after operation, a partial right pneumothorax. The air, however, was promptly absorbed and the right lung completely expanded by the tenth post-operative day. The right diaphragm in the post-operative X-rays occupied an elevated position and as soon as the patient was up and about fluoroscopical examination showed that the right diaphragm was immobile and in high position. Fluoroscopical examination prior to operation showed a mobile diaphragm. The injury to the phrenic nerve evidently occurred during the removal of the tumor. The patient was discharged from the hospital June 23, 1931, three weeks after operation.

Gross pathology.—During the course of the removal of the tumor it was ruptured and there escaped a large quantity of sticky, gelatinous fluid. The weight of the tumor, which on removal was 557 grams, was therefore probably twice this amount. Partially collapsed, the tumor measured 14 centimetres long by 10 centimetres wide by 10 centi-



FIG. 2.

FIG. 2.—Ventral aspect of the tumor after removal. The tumor as noted extended from the xiphoid to the suprasternal notch.



FIG. 3.

FIG. 3.—Section of the tumor showing its solid and cystic portions.

THE TUMORS OF THE STERNUM

metres thick. Measured along the curve of the tumor it measured 21 centimetres long, 10 centimetres wide and 10 centimetres thick. The tumor is intimately associated with the sternum and has risen from this structure. It has perforated the bone so that it presented as a raised elevation on the external surface of the body. This external portion of the tumor is firmly elastic on palpation. The mediastinal portion of the tumor is perfectly encapsulated, the capsule being a structure which varies in thickness up to two to three millimetres. The tumor has undergone extensive degeneration, the degenerated material consisting of a sticky gelatinous fluid. The solid portion of the tumor consists of cartilage intermeshed with masses of calcification.

Gross Pathological Diagnosis.—Chondromyxoma. (See Figs. 2, 3 and 4.) *Microscopical Diagnosis.*—The sections made consist of a completely encapsulated mass of tissue made up of well-formed cartilage surrounding areas of myxomatous degeneration.

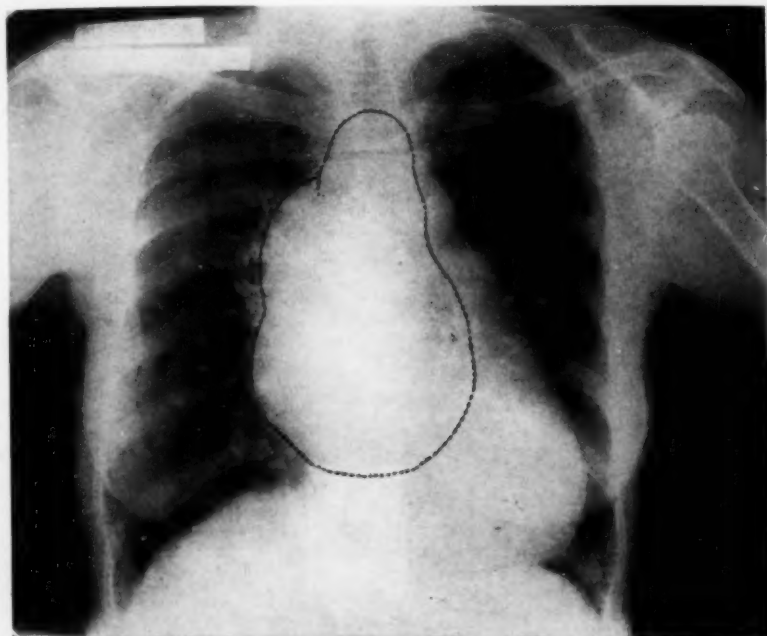


FIG. 4.—The outline of the tumor has been dotted upon the X-ray film to show the extent and relations of the tumor.

Hæmorrhage is also seen here and there throughout the section. The *microscopical diagnosis* is chondromyxoma benign.

Follow-up Notes.—The patient returned for observation July 1, 1931, at which time following note was made:

It is now four weeks since the operation. The wound is completely healed. The patient generally looks well and feels well.

At the site of the operation there is a depression due to the loss of the sternum. With each inspiration this depression sinks slightly, and on expiration again moves forward. The right breast in part fills the defect. Respiration is quiet. The patient's color is good. There is no dyspnoea. Functionally the loss of the lower two-thirds of the sternum seems a very minor matter. Under the fluoroscope the chest moves well, with the exception of the right diaphragm. This occupies a high position and is immobile. There seems no doubt that the right phrenic nerve was traumatized during the removal of the tumor.

Palpating the divided ends of the ribs, the defect in the anterior thoracic wall is

roughly circular in outline and measures 11 centimetres in vertical and $10\frac{1}{2}$ centimetres in transverse diameters. Most of the defect lies to the right of the mid-line. It is



FIG. 5.

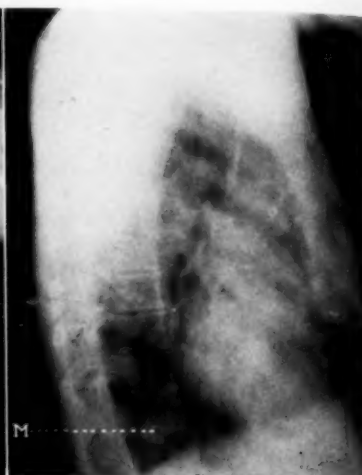


FIG. 6.

FIG. 5.—Antero-posterior X-ray taken ten months after operation. The supposed metastasis in the left costophrenic angle (M) has definitely increased in size. Shadows along the right mediastinum and in the right lung field suggest metastases.

FIG. 6.—Lateral X-ray taken ten months after operation.

apparent on examination that the sternum has not been entirely removed but that the upper segment remains. All of the lower part of the sternum has been removed down to the xiphoid. At the time of the operation the costal cartilages of all the lower ribs



FIG. 7.



FIG. 8.

FIG. 7.—Photograph taken ten months after operation showing operative scar.

FIG. 8.—Lateral photograph taken ten months after operation to show the depression of the anterior thorax.

were divided. Since that time they have come together so as to diminish the epigastric angle.

X-rays of the chest were taken today. The vital capacity this morning was 1,200 cubic centimetres, which is rather low. Weight, 106 pounds.

THE TUMORS OF THE STERNUM

She was seen again October 1, 1931, and the following note made:

Since the last note the patient has gained six pounds. Her color is very much better. She has been quite vigorous—driving her car, *etc.*

Examination of the chest shows the wound perfectly healed with a very good scar. The defect in the anterior thorax has not diminished. It now measures eleven centimetres vertically by eleven centimetres in its greatest transverse diameter. On respiration the region of the defect moves in and out as would be expected. With the patient lying quietly there is very little cardiac pulsation although it can be observed.

On coughing there is considerable bulging in the region of the defect. Respiration is perfectly quiet. There is no shortness of breath on exertion.

X-ray of the thorax taken October 1, 1931, shows the chest perfectly clear. The heart has moved back towards the mid-line although it still is displaced considerably toward the left. The right half of the diaphragm (paralyzed as described in our previous note) does not in this X-ray occupy a high position. Fluoroscopic examination shows that the right diaphragm moves actively and within normal excursions. The paralysis of the right diaphragm noted June 29, 1931, has in the meantime entirely disappeared.

The patient was seen again on April 1, 1932. She had gained twelve pounds since operation. She seemed perfectly well and is leading an active normal life. The X-rays of the thorax show that the presumed metastasis in the lung has increased in size (Figs. 5 and 6 M), but otherwise are negative. Photographs of the patient (Figs. 7 and 8) show the operative scar and the depression of the anterior thorax.

Later reports from the patient were not so encouraging. In May, 1932, she began to complain of "sciatica" in the left leg. The pain radiated along the course of the sciatic nerve and eventually became so severe that she became practically bedridden. Knowing the propensity of these tumors to metastasize she was repeatedly examined and her spine and pelvis X-rayed to determine the presence of metastases. None was found. Later there appeared a nodule at the upper portion of the operative defect to the right of the mid-line which impressed us as either a recurrence in the sternum or a recurrence in the mediastinum presenting at the margin of the bony defect. A similar nodule appeared in the region of the xiphoid at the lower margin of the defect. June 11, 1932, I saw the patient and agreed with Dr. B. N. Carter, who then had the patient in charge, that these nodules, which seemed perfectly circumscribed, should be explored and if possible removed. The operation was performed by Doctor Carter, June 15, 1932. He writes me under date of June 20, 1932, as follows:

"Five days ago I operated on Miss Z. I attacked the upper lump first, making a long skin incision over it, and freed it down to the costal cartilage. I resected the costal cartilage and opened the pleura for it was obvious that I would have to resect a piece of pleura in order to remove the tumor without getting into it. It was a little difficult to say in which pleural cavity I was but I believe I was in the right. Upon introducing my finger I could detect numerous large metastases about the size of golf balls apparently in the mediastinum. The tumor which had appeared on the outside was a continuation of one of these which had grown through the intercostal space. I removed the tumor but I had to cut through portions of it. This I did more for the mental effect upon the patient than with any idea of a cure. I carried through a similar procedure on the lowermost recurrence and found the same state of affairs there. I am afraid she has no chance."

Comments.—The case illustrates the ease with which even very large tumors of this nature may be removed. The sad end-result raises the question as to the origin of the metastases. Previous to the original operation our X-ray studies showed only one possible metastasis, *i.e.*, that in the lower lobe of the left lung. (Fig. 1 M.) This was not examined at the time of

the original operation because the left pleural cavity was not opened. But the mediastinum, the right pleural cavity and the right lung were thoroughly examined at operation and no evidence of metastases found. Is it possible that the numerous nodules in the mediastinum found by Doctor Carter represent implantations due to the rupture of the original tumor during its removal?

DISCUSSION OF TUMORS OF THE STERNUM

Zinninger (*ANNALS OF SURGERY*, vol. xcii, p. 1043, 1930) collected the cases of tumors of the thoracic wall between the time of my studies (1927) and 1930. He found twenty additional cases reported and to this number added eight from the records of the Peiping Medical School. He brings the total number of tumors of the thoracic wall reported in the literature up to 266. I have again gone over the literature with special reference to tumors of the sternum, and, including the case I have just recorded, find thirty-eight cases which are reported and described as tumors of the sternum. Fifteen of them are reported between 1873 and 1890; six between 1890 and 1900; and seventeen between 1900 and the present time. The descriptions of the earlier cases are often faulty and one is left in doubt whether the tumor originated in the sternum or primarily in the clavicle or ribs. As to their point of origin in the sternum, seven are said to have arisen in the gladiolus, nine in the manubrium, two in the gladiolus and manubrium, and one in the xiphoid. The remaining twenty are simply described as arising from the sternum. One of these almost certainly had its origin in the inner end of the clavicle. The pathological descriptions also are often faulty. Thirteen cases are simply designated as sarcomas; seven additional cases are described as myxosarcoma, one; melanosarcoma, one; fibro-myxosarcoma, one; round-cell sarcoma, two; and spindle-cell sarcoma, two. The remaining eighteen cases form pathologically a heterogeneous group: gumma, one; "fibroid" tumor, three; chondroma (including my case), three; carcinoma, two; hypernephroma, two; "malignant thyroid tumor," one; vascular tumor or aneurism, one; and chronic inflammation, one. In one case (Weinlechner) two apparently different tumors of the sternum occurred in the same patient; one a primary chondroma of fifty years' duration, the other a "colloid sarcoma" of three years' duration. In three cases the pathological diagnosis of the tumor is not stated.

Of the thirty-eight tumors of the sternum, therefore, nineteen, or 50 per cent., are primary sarcomas; and to this number probably should be added the three so-called "fibroid tumors." Three or possibly four (12 per cent.) are primary cartilaginous tumors (chondroma; enchondroma; chondromyxoma), one is a gumma, and one is a chronic inflammatory lesion. The remaining seven tumors (18 per cent.) in which a diagnosis is stated are secondary, metastatic lesions. Of these, three were pulsating tumors and the primary diagnosis was aneurism. In one, the diagnosis of hypernephroma was con-

THE TUMORS OF THE STERNUM

firmed by biopsy, in a second, the diagnosis of hypernephroma was established by necropsy; in the third, a positive diagnosis was not established.

It will be seen from this summary that the primary cartilaginous tumors of the sternum are rare, the case just described by me being the third or possibly the fourth to be reported.*

Of the thirty-eight cases, thirty-four were subjected to a more or less radical operation, two to a biopsy for diagnostic purposes, and one to radium treatment. One was not treated.

Of the thirty-four cases subjected to a more or less radical operation, eight died within fifteen days of the operation, and twenty-three recovered. In three cases neither the immediate nor late result of the operation is given. Of the twenty-three cases which recovered, three failed to show evidence of recurrence from one to two years and were living at the time of the report. Nine cases presented recurrences from one month to two years after operation from which six died. In ten cases the end-result is not given. The single case which is known from the reports in the literature to have survived beyond a two-year period is one, not of tumor, but of chronic inflammation. Of the three cases of enchondroma subjected to operation, one died five days after operation from pyæmia, and two showed recurrences or metastases within a year after operation.

A brief summary of the cases of tumor of the sternum thus far reported is appended.

CASE I.—Holden: Brit. Med. Jour., vol. xi, p. 358, 1878. A woman, aged fifty-two, with a sarcoma involving the gladiolus. At operation the tumor was partially removed. Details of the operation are lacking. Neither the immediate nor the late results of the operation are given.

CASE II.—König: Centralb. f. Chir., No. 42, 1882. A woman, aged thirty-six, with a sarcoma of the sternum. At operation the gladiolus, a part of the manubrium, the second to the eighth ribs on the left and the ends of the cartilages on the right were resected. Both internal mammary arteries were ligated. The pericardium was opened. Both pleuræ were opened (openings probably small) causing slight respiratory difficulty and tachycardia. The management of the bilateral pneumothorax is not stated. The patient recovered but died two years later from recurrences in the lungs. Paget commenting upon this case states that the patient died one year after operation from rheumatic fever.

CASE III.—Küster: Berlin klin. Wchnschr., p. 127, 1882. A man, aged thirty, with a tumor, later diagnosed a gumma, of the sternum. At operation the right half of the gladiolus and the third and fourth ribs were resected. One pleural cavity was slightly opened. Whether or not respiratory or cardiac disturbances followed is not stated. The patient recovered from the operation. The late result is not given.

CASE IV.—Pfeiffer: Beitr. z. Kennt. d. Sternal Tumoren, Halle, 1884. A man, aged forty-five, with a sarcoma of the gladiolus. At operation, the gladiolus and the second, third and fourth ribs right and left were resected. The right pleura was opened and probably also the pericardium. The patient developed an acute pericarditis and

*The fourth case I have in mind is that of Gangolph et Tixier in Lyon Chir., vol. ii, p. 112, 1909-1910, under the title of "Enorme Enchondrome de la fourchette sternale. Resection de la moitié supérieure du Sternum, etc." Unfortunately, this reference at the moment is not available.

pleuritis and died on the sixth post-operative day. The autopsy showed other tumors on the fourth rib and metastases in the aortic glands, liver and right kidney.

CASE V.—Bardenheuer: Deutsch. Med. Wchnschr., vol. xi, p. 688, 1885. A woman of unstated age with a "fibroid" tumor of the manubrium. At operation the manubrium, two-thirds of the clavicle and the second and third ribs were resected. There are no details regarding the opening of the pleura. The patient recovered. The late result is not given.

CASE VI.—*Ibid.*—A man of unstated age with a sarcoma involving the manubrium but presumably arising from the inner end of the clavicle. At operation the manubrium, two-thirds of the clavicle and the first and second ribs were resected. The internal jugular vein was torn during the operation and the right innominate, subclavian and internal and external jugular veins ligated. The patient recovered from the operation. The late result is not stated.

CASE VII.—*Ibid.*—A patient with a tumor presumably of the manubrium. The nature of the tumor is not stated. At operation the manubrium was resected. The patient recovered. No other details given.

CASE VIII.—*Ibid.*—A patient with a tumor presumably of the manubrium. The nature of the tumor is not stated. At operation the manubrium was resected. The patient died. No other details are given.

CASE IX.—*Ibid.*—A patient with a tumor presumably of the manubrium. The nature of the tumor is not stated. At operation the manubrium was resected. The patient died. No other details are given.

CASE X.—*Ibid.*—A woman with a retrosternal "fibroid" tumor involving the manubrium, part of the gladiolus, the first and second ribs and the inner end of the clavicle. At operation these structures were resected. The patient recovered. The late result is not given.

CASE XI.—*Ibid.*—A patient with a retrosternal "fibroid" tumor involving the manubrium, part of the gladiolus, the first and second ribs and the inner end of the clavicle. Resection of these structures. The patient recovered. The late result is not given.

CASE XII.—Jaenel: Inaug. Diss. Erlangen, 1887. A girl of twelve years with a sarcoma of the manubrium. At operation the manubrium and the first and second ribs were resected. The retrosternal tissues were found involved and were cauterized with the actual cautery and nitric acid. The patient recovered. There was no recurrence at the end of one year.

CASE XIII.—Dudon: Jour. de Med. de Bordeaux, June 1, 1890. A woman, twenty-eight years of age, with an enchondroma of the gladiolus. A previous operation, the details of which are scanty, had been performed twenty-seven months before. At the second operation, eight months after the first, the manubrium, part of the gladiolus and the first and second ribs were resected. The wound suppurred. The patient recovered. The last report indicated recurrences in the pectoral and sternomastoid muscles.

CASE XIV.—Mazzoni: Cited by Dudon above. A man, fifty-five years of age, with a myxosarcoma of the gladiolus. At operation the gladiolus and the second, third and fourth ribs were resected. The patient died fifteen days after operation from pneumonia. No other details given.

CASE XV.—Graves: Med. News, vol. lxii, p. 241, 1893. A woman, aged forty-four, with a sarcoma of the gladiolus. At operation the gladiolus and the second, third, fourth and fifth ribs were resected. The history relates that a breast had been removed twenty-two months previously for carcinoma which casts some doubt upon the diagnosis of sarcoma. The patient recovered from the operation. The late result is not given.

CASE XVI.—Doyen: Arch. Prov. de Chir., vol. iv, p. 633, 1895. A man, aged thirty-seven, with a sarcoma of the manubrium. At operation the manubrium, parts of

THE TUMORS OF THE STERNUM

both clavicles and the first rib were resected. Neither pleura was opened. The patient recovered. The late result is not given.

CASE XVII.—Mynter: *ANNALS OF SURGERY*, vol. xiii, p. 96, 1891. A woman, aged twenty, with a melanosarcoma of the gladiolus. At operation the gladiolus and the third, fourth and fifth ribs were resected. The subclavian and axillary glands on both sides were removed. The patient recovered but died one year later presumably from metastases.

CASE XVIII.—Keen: *Med. and Surg. Reporter*, vol. lxxvi, March, 1897. A woman, aged twenty-eight, with a sarcoma of the manubrium. At operation, the manubrium, one-third of the clavicle, first rib and one-third of the sternomastoid muscle were resected. The wound suppurated. The patient recovered. There was no evidence of recurrence fifteen months after operation. Later reports not available.

CASE XIX.—*Ibid.*—A woman, aged forty-four, with a carcinoma of the manubrium and gladiolus. The condition was secondary to carcinoma of the breast. At operation a partial resection of the manubrium, gladiolus and second and third ribs was accomplished. The patient recovered from the operation but died five months later.

CASE XX.—Weinlechner: *Bericht d. K.K. Krankanstl. Rud. Stift in Wien*, p. 124, 1873. A man, aged fifty-eight, who is stated to have had two distinct tumors of the sternum, one, a primary chondroma of fifty years' duration, the other a colloid sarcoma of three years' duration. At operation what appears to have been only a local excision of the tumors was undertaken. The wound became infected and the patient died on the fifth post-operative day from pyæmia.

CASE XXI.—König: *Inaug. Diss.*, 1894. A man, aged fifty-nine, with a sarcoma the size of a "fist" involving the sternum. At operation the sternum and the second to the fifth ribs on both sides were resected. During the operation an opening the size of a "five-mark piece" was made in the right pleura. There was at first no respiratory or cardiac upset but subsequently dyspnoea and feeble pulse appeared. The patient died. At necropsy he was found to have brown atrophy of the heart.

CASE XXII.—Amburger: *Beitr. z. Klin. Chir.*, vol. xxx, p. 770, 1901. A man, aged forty-seven, with a round-cell sarcoma of the sternum. The tumor measured three by nine by eleven centimetres in its various diameters. At operation the manubrium and the first and second ribs were resected. Both pleuræ were opened during the operation but the size of the openings is not stated. No untoward symptoms followed. The patient died three days after operation.

CASE XXIII.—*Ibid.*—A man, aged thirty-seven, with a round-cell sarcoma (size of goose egg) of the sternum. At operation the gladiolus and three ribs were resected. The pleura was not opened. The patient recovered but subsequently died from metastases.

CASE XXIV.—*Ibid.*—A woman, aged twenty-two, with a spindle-cell sarcoma (size of apple) of the sternum. At operation the manubrium and the first and second ribs were resected. The left pleura was opened but the size of the opening is not stated. No upset followed. The patient recovered and at the expiration of two years there was no evidence of recurrence.

CASE XXV.—*Ibid.*—A man, aged forty, with a fibromyxosarcoma involving the sternum, the mediastinum and the pectoral muscle. The tumor was of seventeen years' duration and had attained the size of a "fist." At operation the manubrium and the second and third ribs were resected. The left pleura was opened but no disturbance followed. The patient recovered. One year later he died from a hæmorrhage from a recurrence which had reached the size of a child's head.

CASE XXVI.—Morestin: *Bull. de la Soc. Anat. de Paris*, vol. lxxvii, p. 414, 1902. A woman of unstated age with a sarcoma of the sternum. Her breast had been amputated for sarcoma seven months previously. At operation the manubrium was resected. The result is not given.

CASE XXVII.—Mayer: *Jour. Med. de Brux.*, vol. ix, p. 146, 1904. A woman, aged thirty-eight, with a sarcoma of the sternum. At operation the sternum and the three

upper ribs were resected. A double pneumothorax was produced during the operation, the effects of which are not stated. The patient developed empyæma and died nine days after operation.

CASE XXVIII.—Isaacs: *Am. Jour. Surg.*, vol. xxiii, p. 291, 1909. A woman, aged forty-six, with a spindle-cell sarcoma of the sternum (size of hen's egg). At operation the sternum below the level of the second costal cartilage was resected. A pneumothorax was produced but no details are given. Pneumonia complicated the convalescence. The patient recovered but presented a recurrence and metastases one month after operation.

CASE XXIX.—Lamphear: *Surg., Gynec., and Obst.*, vol. xiv, p. 619, 1912. A woman, aged sixty-one, with a carcinoma of the sternum. At a two-stage operation the manubrium and a part of the clavicle were resected. A pneumothorax was not produced. The patient recovered. The late result is not stated.

CASE XXX.—Richardson: *Brit. Med. Jour.*, vol. i, p. 985, 1913. A man, aged twenty-six, with a chondroma of the manubrium. The tumor was of long duration but had recently grown rapidly. At operation the manubrium was resected. The patient recovered. The late result is not stated.

CASE XXXI.—Le Jars: *Le Semaine Med.*, vol. xxxiv, p. 16, 1914. A man, aged forty, with a sarcoma, four to five inches in diameter, involving the xiphoid. At operation the xiphoid was resected. The result is not given.

CASE XXXII.—Hedblom: *Arch. Surg.*, vol. iii, p. 56, 1921. A woman, aged fifty-three, with a tumor of the manubrium. At operation the manubrium was resected. The tumor proved to be the result of a chronic inflammatory process. The patient recovered. There has been no recurrence.

CASE XXXIII.—McLeod and Jacobs: *Med. Rec. N. Y.*, vol. c, p. 979, 1921. A man, aged fifty-four, with a pulsating tumor, the size of "one-half an orange," involving the sternum. A diagnosis of aneurism was first made. A biopsy for diagnostic purposes showed the tumor to be a hypernephroma. No further operation done. The patient died some time later. An autopsy was not obtained.

CASE XXXIV.—*Ibid.*—A man, aged sixty-nine, with a pulsating tumor, $3\frac{1}{2}$ by 6 inches in size, involving the sternum. A diagnosis of aneurism was made. The patient died some six weeks after coming under observation. The autopsy showed a hypernephroma with a metastasis in the sternum.

CASE XXXV.—Maingot: *Brit. Med. Jour.*, vol. i, p. 140, 1926. A woman, aged seventy-three, with a tumor 3 by $2\frac{1}{2}$ inches in diameter involving the manubrium. A biopsy showed a "malignant thyroid tumor." Clinically, there was no evidence of thyroid disease. The result is not stated.

CASE XXXVI.—Griffith: *Lancet*, London, vol. ii, p. 991, 1902. A patient with a large sarcoma of the sternum. At operation the sternum from the second to the seventh costal cartilages was resected. The growth was not completely removed. A large opening in the pleura was produced which gave rise to slight shock. The patient recovered from the operation but died four months later, presumably from a continuance of the disease.

CASE XXXVII.—Zininger: *ANNALS OF SURGERY*, vol. xcii, p. 1043, 1930. A male Chinese, aged forty-seven, with a tumor the size of a hen's egg involving the sternum. The tumor pulsated and was thought to be either a vascular sarcoma or an aneurism. A radium pack was applied but without improvement. The outcome is unknown.

CASE XXXVIII.—Heuer.—See above.

THE SURGICAL TREATMENT OF MEDIASTINAL TUMORS

REMOVAL OF CYSTIC AZYGOS LOBE FROM POSTERIOR MEDIASTINUM

BY STUART W. HARRINGTON, M.D.

OF ROCHESTER, MINN.

THE incidence of intrathoracic tumors is probably no greater now than it has ever been, but in recent years they are being recognized more frequently, due to the marked improvement that has been made in methods of thoracic diagnosis, especially since the use of Röntgen-rays. Early diagnosis of these tumors, before the growth has made serious inroads on the patient's general condition, has been the greatest aid to their surgical removal, and study of such proved cases has given a different conception of the type of lesion found in this region as well as of the prognosis. The older belief was that most of these growths were malignant, and that only conservative treatment was justified, because surgical treatment was an extremely hazardous procedure. The lack of response in so many of these cases to conservative treatment has encouraged surgical intervention with the view of complete removal of the growth, and the marked advancement in methods of surgical technic has made operative removal a relatively safe procedure. Microscopical study of the lesions removed has shown that a large percentage of intrathoracic tumors are benign.

A relatively high percentage of intrathoracic growths have their origin in the mediastinum. Because of the many different tissue elements in this space, it has the potential possibility of presenting almost any type of neoplasm. In my experience of thirty-eight cases in which intrathoracic new growths were removed by operation, twenty-three (61 per cent.) were in the anterior or posterior mediastinum. Microscopical study of these twenty-three cases disclosed that eighteen (78 per cent.) were benign tumors of the following types: eight were neurofibromas, in three of which there was lipoid degeneration; two were cellular fibromas; seven were teratomas, one of the dermoid type and one presenting sufficient organoid structure to be designated as a parasitic foetus, and one, the eighteenth, a congenital cyst of the lung. The last case is reported in this paper. The remaining five tumors of the mediastinum (22 per cent.) were malignant, of which one tumor was a squamous-cell epithelioma which probably arose by malignant degeneration of a dermoid tumor of the anterior mediastinum; three tumors were fibrosarcomas, two of which were probably primarily benign tumors, and one, the fifth, was an adeno-carcinoma of intrathoracic thyroid tissue, with erosion of the spine. All mediastinal tumors are potentially malignant. The high percentage of benign tumors in this series is probably due to removal of the growth, before it had undergone malignant change. The clinical history of three of the five patients who had malignant tumors sug-

gested that the tumor had been benign at the onset and had undergone malignant degeneration.

Tumors that remain benign often attain enormous size, and may cause death from mechanical pressure on the numerous important structures in the potential spaces designated as the mediastinum. These structures either control, or are closely associated with, respiration; circulation of arterial and venous blood and lymph; deglutition, and functional innervation of organs lying outside the thorax. Inasmuch as the mediastinum is only a potential space, growths arising in this region will impinge on the anatomically adjacent structures, depending on the situation of the lesion, such as the lungs, vertebræ, diaphragm and structures at the base of the neck. Because of the important structures contained in the mediastinum it is of paramount importance that these tumors be recognized and treatment instituted before the growth has caused serious and permanent injury to these vital structures, as well as disturbing the function of all the viscera within the thorax.

There is great variation in the subjective symptoms produced by mediastinal neoplasms. The symptoms are dependent on the type of growth, but more on the situation than on the size of the tumor. They are due to pressure or infiltration of the involved or surrounding structures in the region invaded, and on the amount and severity of disturbed function of intrathoracic organs. If the symptoms appear early, it may be possible to make a diagnosis by the history and general examination only, but it is extremely rare more than to suspect the presence of a tumor on the basis of these observations. Most cases can be definitely diagnosed only by aid of Röntgen-rays, whether or not they produce symptoms, and regardless of physical findings.

The most common symptoms and signs which cause the patient to consult the physician are as follows: Pain; dyspnoea; cough; various degrees of cyanosis caused by pressure on the lungs, heart, great vessels or nerves; displacement of the heart from pressure; dilatation of the veins over the thorax, and distention of the jugular vein from pressure on the superior vena cava; dysphagia from extrinsic pressure on the œsophagus; changes in the voice from pressure on the recurrent laryngeal nerve; unilateral sweating and flushing of the face associated with enophthalmus, visual disturbance, inequality in the size of the pupils, and ptosis of one eyelid from pressure on the sympathetic nerves; nerve pain, root pain, and herpes from pressure erosion of the spinal column and spinal cord; difference in size of the two sides of the thorax; decrease or absence of motion of one side of the thorax during inspiration; loss of weight; anorexia; pyrexia, and evidence of pleural effusion or empyæma.

Pain is probably the most significant symptom in the clinical distinction between an early malignant lesion and a benign lesion. From malignant growths of small size the pain is often very severe, and may be more or less constant, but with acute exacerbations at irregular times, usually most severe at night.

Benign tumors may often attain great size without producing pain other

MEDIASTINAL TUMORS

than a dull ache or a sense of pressure accompanied by dyspnoea on exertion. Benign, anterior mediastinal tumors usually present more subjective symptoms than benign posterior tumors because of the limited space anteriorly, and these tumors are usually fixed to the heart and great vessels. The most common benign anterior mediastinal tumors are teratomas, which often produce pain as a result of inflammatory irritation associated with respiratory infections; the diagnosis commonly is pleurisy or pneumonia. The most common growths in the posterior mediastinum are neurofibromas and cellular fibromas, which may attain considerable size without causing pain unless the tumor is of the dumb-bell type, causing erosion of the spinal column with associated root pain and symptoms referable to the spinal cord, depending on the portion of the spine involved.

Dyspnoea is one of the most common symptoms of benign or malignant tumors, is usually present with early lesions, and is most noticeable on exertion. It is caused by pressure on the lungs, particularly at the hilum, also by pressure on the heart, great vessels, and nerves. It may be constant or paroxysmal, and is often the only subjective symptom.

Cough is a frequent early symptom of malignant lesions, and it is often paroxysmal and of a hoarse or brassy type. It may be nonproductive, but usually is associated with expectoration of mucus or blood. The type of expectoration may be of great diagnostic importance, as in the presence of dermoid or teratoid growths which have ruptured into a bronchus, with expectoration of sebaceous material, hair, and occasionally tumor tissue and pus from secondary infection. Expectoration of this material often occurs at night, and may be associated with violent attacks of coughing and pain simulating attacks of strangulation.

Horner's ocular syndrome was noted in three cases, in all of which the growths were malignant, which would suggest that the syndrome was due to malignant infiltration rather than to pressure on the sympathetic nerves. I have removed several benign tumors of much larger size from the same region in cases in which Horner's syndrome was not present.

The physical signs are often helpful in determining the presence of a lesion but are unreliable as to its extent or character. Vocal fremitus will usually be increased over the tumor, and with this there is usually an area of definite dullness and absence of breath sounds. In the presence of anterior mediastinal tumors the heart is often displaced and the sounds are transmitted over a wide area. All of the usual physical signs of regions of consolidation in the thorax may be absent and a tumor of considerable size may be present but produce no evidence either by symptoms or on general examination.

In most instances, the greatest amount of information that can be expected to be obtained from the clinical history and the physical signs is that of the probable presence of a mediastinal tumor, and its approximate situation. In order to determine accurately the position and size of the growth and its relation to the normal content of the mediastinum and thorax, resort must be had to other methods of examination. The most

important of these is röntgenological examination of the thorax. This should be made in the anteroposterior, oblique, and true lateral positions, and its value is greatly enhanced by stereoscopic films. In certain cases, additional information can be obtained from röntgenological examination after establishment of artificial pneumothorax, after injection of the bronchial tree with iodized oil, or after introduction into the œsophagus of a preparation of barium. Fluoroscopical examination is of value in determining the relation of the tumor to the surrounding normal structures, and in determining whether it is encroaching on, or is causing, impairment of function of these structures. It is also of importance in the differential diagnosis of tumors and aneurism.

Bronchoscopical examination is of value in ruling out the presence of a primary intrabronchial lesion, or in determining whether there is encroachment of an extrinsic growth on the lung. Œsophagoscopical examination is of value in ruling out the presence of a primary lesion of the œsophagus, or in determining if there is encroachment of an extrinsic lesion on the œsophagus.

Thoracoscopical examination may be advisable in selected cases of posterior mediastinal tumor in which the growth projects well into the thoracic cavity. In this way, the situation of the tumor can be determined, and in some instances a specimen of the tumor may be removed for microscopical examination. However, in most of these cases, I prefer to perform exploratory thoracotomy. In cases of anterior mediastinal tumor, it is rarely, if ever, advisable. Diagnostic thoracentesis, with an aspirating needle, may be justified in certain rare cases, such as when the available evidence is that of a cyst adherent to the thoracic wall, or to aid in distinguishing between such a cyst and an encapsulated accumulation of fluid in the pleural cavity. This procedure is rarely, if ever, advisable in cases of anterior mediastinal tumor, because of the danger of mediastinal infection entailed, in any case, at inserting a needle into the mediastinum, and especially because of the possible risk of injury to an aneurism of the arch of the aorta.

In some cases, differential diagnosis of malignant and benign disease remains in doubt after all of the armamentarium of modern thoracic diagnosis has been exhausted. In some cases of malignant disease there may be involvement of the regional superficial lymph-nodes, and one of these can be removed for microscopical examination to establish the correct diagnosis, but in many cases there is no enlargement of regional lymph-nodes. In some cases of this latter group, in which the tumor is unilateral and the available evidence is more characteristic of a malignant growth of the type of lymphoblastoma, treatment of the growth with Röntgen-rays is often of diagnostic value, for these tumors are radiosensitive and will appreciably diminish in size from a week to ten days after irradiation. In cases of benign tumor there will be no appreciable change in the size or contour of the tumor following irradiation. The differential diagnosis of mediastinal tumor and aneurism of the aorta usually can be made on the basis of the clinical symp-

MEDIASTINAL TUMORS

toms which are associated with aneurism, and by means of fluoroscopical examination of the thorax. In fluoroscopical examination, care must be exercised not to confuse the pulsation of an aneurism with that of the transmitted pulsation from the arch of the aorta onto the tumor. In those cases in which the diagnosis cannot be established even after all available methods have been utilized, exploratory thoracotomy is indicated, depending on the patient's general condition.

The chief problems associated with surgical removal of mediastinal tumors are concerned with the danger of pulmonary collapse, with mediastinal flutter resulting from open pneumothorax, and the difficulty of access through the bony encasement of the thorax. The first of these hazards has been greatly diminished by the use of differential air-pressure during the operation. The second is entirely a technical problem, and methods of approach are continually being improved and perfected.

Surgical indications depend on the findings in each case. Patients who are selected for surgical intervention should be placed in the hospital under observation and pre-operative preparation for approximately one week before operation. After bronchoscopical or thoracoscopical examination has been made, the operation should be delayed for at least three to five days. I believe that the operative risk is decreased by establishment of artificial pneumothorax approximately five days before operation, to permit the patient to become accustomed to unilateral partial pulmonary collapse, and decreased vital capacity. In my series of twenty-three cases, including anterior and posterior mediastinal tumors, preliminary artificial pneumothorax was established in eleven. In some instances it will be impossible to establish artificial pneumothorax because of adhesion of the lung to the tumor, or to the thoracic wall, which will prevent collapse of the lung. In the pre-operative period the patient should be given at least 3,000 cubic centimetres of fluid daily.

I prefer to use intratracheal anaesthesia under positive pressure. I have operated with intrapharyngeal anaesthesia, with the closed mask, and without positive pressure of the anaesthetic agent, without harmful results. It is probable that intrapharyngeal anaesthesia would be satisfactory in most cases in which one pleural cavity is opened, but it is never possible to determine before operation what emergency may arise, or when the opposite pleural cavity may be opened unavoidably. I believe that anaesthesia by intratracheal insufflation, and administered with apparatus for positive pressure, is the safest method in most cases; this method was used in most of the twenty-three cases mentioned. The anaesthetic agents were ethylene and ether or ethylene alone, in all cases. Many of these operations are long and tedious, and it is important to ventilate and reestablish circulation by fully expanding the lung every three to five minutes during the operation. The amount of pressure used is gauged by a water manometer on the positive-pressure apparatus. The lung is fully inflated at the completion of the operation. A

suction pump is applied to the intratracheal catheter during its withdrawal to remove any mucus which may have accumulated in the trachea.

The surgical approach through the thoracic bony cage depends on the site and size of the tumor. To reach anterior mediastinal tumors, it may be through the anterior or posterior thoracic wall. Nine of the twenty-three mediastinal tumors in my experience were in the anterior mediastinum. In two of these cases the tumor was approached through the anterior thoracic wall, and in one of them the clavicle was cut in order to approach the tumor at the apex. In the remaining seven cases, the approach was made through the posterior thoracic wall through a posterolateral incision around the vertebral border of the scapula, and entering the pleural cavity through the deep layer of periosteum after resecting one rib. The vertical level of the incision in the pleura depends on the situation of the tumor; that is, whether it is high or low in the mediastinum. If more exposure is necessary in order to remove the tumor, the ribs can be cut close to the spinal column, both above and below the resected rib, together with the intercostal muscles, until sufficient exposure has been obtained to remove the growth from its attachment and to deliver the tumor through the wound. At completion of the operation the cut ends of the ribs are sutured by drilling through them and suturing them together with chromic catgut. In all of the fourteen cases in which the tumor was in the posterior mediastinum, the posterior approach was used. I prefer this method of approach in all cases of mediastinal tumor, unless the tumor causes so much pressure in the anterior mediastinum that the growth is firmly fixed to and has caused marked deformity of the thoracic wall. In some of these cases it may be advisable to make the incision over the site of the tumor. In nineteen cases the tumor was removed by transpleural operation. In four cases it was removed by extrapleural operation; two of these tumors were removed through an anterior incision, and two through a posterior incision. A posterior, extrapleural operation was attempted in several other cases, but such an operation is rarely possible because of adhesions of the pleura to the tumor; these were usually so firm that the pleura was ultimately entered before the tumor could be completely removed, thus subjecting the patient to all of the dangers of open pneumothorax, and in addition to the probability of extensive pleural effusion due to the wide separation of the pleura from the thoracic wall. I believe that there is less risk in performing an initial transpleural operation in most cases. In all cases, the tumor was completely removed in a one-stage operation. This I believe to be the operation of choice, for the technical difficulties are usually increased by operations in multiple stages, which increase the danger of the operative procedure.

The blood-pressure should be taken every five minutes during the operation. When there has been a fall of ten millimetres of mercury in the pulse-pressure, physiological solution of sodium chloride or solution of acacia is given intravenously. If the pulse-pressure drops twenty to thirty millimetres of mercury, transfusion of blood is given.

MEDIASTINAL TUMORS

Post-operative care is very important. Maintenance of bodily heat is essential, both when the patient is on the operating table, and after operation. The most significant immediate complication is dyspnoea with cyanosis. If this occurs, the patient is placed immediately in the oxygen chamber. This often proves to be a life-saving procedure, for it tides the patient over the critical period of decreased vital capacity of the lungs. This was particularly exemplified in one case, in which a large teratoma was removed from the anterior mediastinum; the growth had extended into the right thoracic cavity, causing almost complete collapse of the right lung and displacement of the heart into the left thoracic cavity from pressure. Because of marked decrease in vital capacity following operation it was necessary to keep the patient in the oxygen chamber for three weeks. Five attempts were made to remove the patient from the oxygen chamber before such removal was finally accomplished after the gradual decrease of the percentage of oxygen over a period of ten days. The oxygen chamber was used in sixteen of my twenty-three cases. Later complications are pleural effusion and empyæma. In practically all cases pleural effusion develops, but in a few of the cases aspiration is not required. In about a third of the cases pleural effusion will disappear after one aspiration, and in the remaining third it will require repeated aspiration. The frequency and persistence of pleural effusion depend on the type of tumor and the amount of trauma to the pleura. In cases of teratoma, pleural effusion is most likely to develop and may result in empyæma. Empyæma complicated the convalescence in five cases of this series of twenty-three; in all five cases drainage was accomplished by the closed method. In one case, subsequent open operation was required. In one case, convalescence was complicated by the development of osteomyelitis of a rib, with formation of a sequestrum, for which further resection of the rib and removal of the sequestrum was required. Convalescence was delayed in these cases, but all the patients recovered.

There were three operative deaths. One patient, who had a neurofibroma, died on the fourth day after operation from pneumonia and an associated bloody pleural effusion. The bloody pleural effusion resulted from diffuse oozing from the bed of the tumor where it had been adherent to the lung. The adhesions were probably the result of extensive Röntgen therapy, to which the patient had been subjected prior to her admission to the clinic because the tumor was thought to be malignant. The tumor did not become smaller, and I believe that any mediastinal tumor which does not undergo some reduction in size within the first week or ten days after irradiation, should not be treated further with Röntgen-ray if surgical intervention is contemplated. The second death occurred six days after operation, as a result of bronchopneumonia and hæmorrhage into the spinal cord. The tumor was a neurofibroma which had been present for more than five years. The patient was practically symptomless until three to six months before admission. A congenital condition of the heart with coarctation of the aorta also was present. At operation it was found that the tumor had eroded

through the vertebræ, causing pressure on the spinal cord, with marked dilatation of the vessels in the spinal cord. This dilatation of vessels was probably primarily due to coarctation of the aorta, and was augmented by pressure from the tumor. Following the operation, hæmorrhage developed from the vessels in the cord, requiring laminectomy in twenty-four hours. The erosion of the spinal column in this case exemplified the serious effect that benign tumors may have on the surrounding structures, which materially increases the operative risk and emphasizes the importance of early removal of the growths. The third death took place on the seventh day after operation, from cerebral embolism. The case was one of malignant degeneration of an anterior mediastinal dermoid. The possibility of malignant degeneration of tumors of this type manifests the importance of early diagnosis and removal.

Twenty patients recovered from operation; three died subsequent to operation; the tumors in these cases were malignant and the patients died from recurrence. One patient, who had a sarcoma which probably originated in the vertebra, died five months after operation from recurrence; two patients who had fibrosarcomas, and whose histories indicated benign tumors at the onset, died of recurrence, one, two and one-half years after operation, and the second, six months after operation. One patient who had a carcinoma of the thyroid gland with metastasis into the mediastinum is living at the present time, two years and four months after operation, but has a recurrence. Sixteen patients, all of whom had benign tumors, are living and completely relieved of symptoms from three months to six years after operation.

Cases of benign tumors are the most gratifying from a surgical standpoint, for the risk is not great if the tumors are removed before they have become so large as to cause pressure on the surrounding structures. If the patient survives the operation, complete cure is obtained. The frequency with which these tumors become malignant is the most significant indication for their early surgical removal. Because of the difficulty in establishing a definite clinical diagnosis, I believe that exploration should be made in all cases, unless the clinical evidence is that a hopeless, inoperable condition exists.

Following is a report of a recent case which is of unusual interest because of the uncommon occurrence of an azygos lobe and the infrequency with which such a lobe is the site of a pathological process. I have been unable to find in the literature a report of a similar case.

REPORT OF CASE.—A woman, aged thirty-seven years, first came to the clinic September 17, 1930, at which time she was found to have a large substernal goitre; this was removed September 23, 1930. In the course of her examination at this time, she complained of an indefinite pain in the upper right posterior portion of the thorax. Röntgenological examination (Figs. 1, 2 and 3) revealed fluid in an azygos lobe, the upper level of which was between the sixth and seventh ribs. There were no other subjective symptoms. She returned for observation December 31, 1931, at which time she stated that she had done very well following thyroidectomy, until April, 1931, which

MEDIASTINAL TUMORS

was seven months after operation, when severe respiratory infection developed, associated with a sore throat. This was accompanied by increase in temperature and severe cough. She had never entirely recovered from the cough. The expectoration varied in quantity and was of yellowish, pus-like material which was very thick and tenacious. It varied in quantity from two to six ounces (60 to 180 cubic centimetres) daily, and was usually very difficult to raise. Often she coughed for a long period before this material could be expectorated. She believed the difficulty was due to the thick, sticky character of the material. There had never been any hæmorrhage, and only moderate pain, which was in the upper right portion of the thorax and was noted when there was difficulty in expectorating the mucoid material. She had been unable to work since the onset of her cough because of weakness and fatigue. She had lost six and one-half pounds in the previous six months.

Examination revealed systolic blood-pressure of 122 millimetres of mercury, and diastolic of 94. The pulse-rate was 104 beats each minute, and the temperature 98.1° F. Repeated examinations of sputum were negative for organisms of tuberculosis and actinomycosis. There was dullness to percussion, and many loud, bubbling râles were heard in the right portion of the thorax, at the level of the third rib anteriorly and from the seventh rib posteriorly to the apex. Röntgenological examination revealed a dense tumor in the upper right mediastinal region, corresponding in situation with the position of an azygos lobe, extending from the seventh to the second rib posteriorly, filling the entire posterior mediastinum and extending across the median line to the left border of the aorta. In the lateral stereoscopic view there was a dense, fusiform shadow in the midst of the upper right portion of the thorax, overlying the shadow of the spinal column. The lower border of the shadow gave evidence of communication between the structure which caused the shadow and a bronchus, at the hilum. A tentative diagnosis of infected congenital cystic tumor of the lung, probably a cystic azygos lobe, was made. Two bronchoscopical examinations were made, and at the first examination, January 5, 1932, a large quantity of pus was found exuding from the bronchus of the right upper lobe. It was impossible to remove all of the pus-like material, for it continued to pour down regardless of continuous aspiration. It apparently came from the posterior division of the bronchus of the right upper lobe. Lipiodol, thirty cubic centimetres, was injected into the bronchus of the upper right lobe. Bronchoscopy was done again January 11; a large amount of pus-like material was found exuding from the bronchus of the right upper lobe, and about 300 cubic centimetres of this material were aspirated and sent for bacteriological examination, culture, and inoculation of guinea-pigs. No organism was found in the stained specimen, nor was any growth obtained from the culture. After a requisite time, the guinea-pig was examined, but no evidence of tuberculosis was found. The patient was partially relieved of cough and expectoration for about twenty-four hours following the bronchoscopical aspiration, after which time the cough was the same as before. She was placed in the hospital under observation for a few days. She had no fever, but the cough and expectoration became gradually worse, and there seemed to be more pain in the upper right portion of the thorax, posteriorly. Surgical intervention was advised.

January 16, 1932, transpleural, posterior mediastinotomy was performed under intratracheal anæsthesia with ethylene. The posterior two-thirds of the sixth rib were removed, from the spine of the vertebra laterally, the fifth and fourth ribs were drilled and cut (Figs. 4 and 5), and the right pleural cavity was entered through the inner layer of periosteum of the sixth rib. There was a large cyst in the right lung, in the same relative position as an azygos lobe, involving the upper posterior part of the mediastinum, and involving about two-thirds of the upper right portion of the thorax. There was partial collapse of the upper and posterior parts of the right lung, which were very adherent to this cystic mass, and completely surrounded it laterally. The median portions of the upper and posterior parts of the lung were separated from the tumor, which was firmly adherent to the upper lobe, and had to be cut from it with a

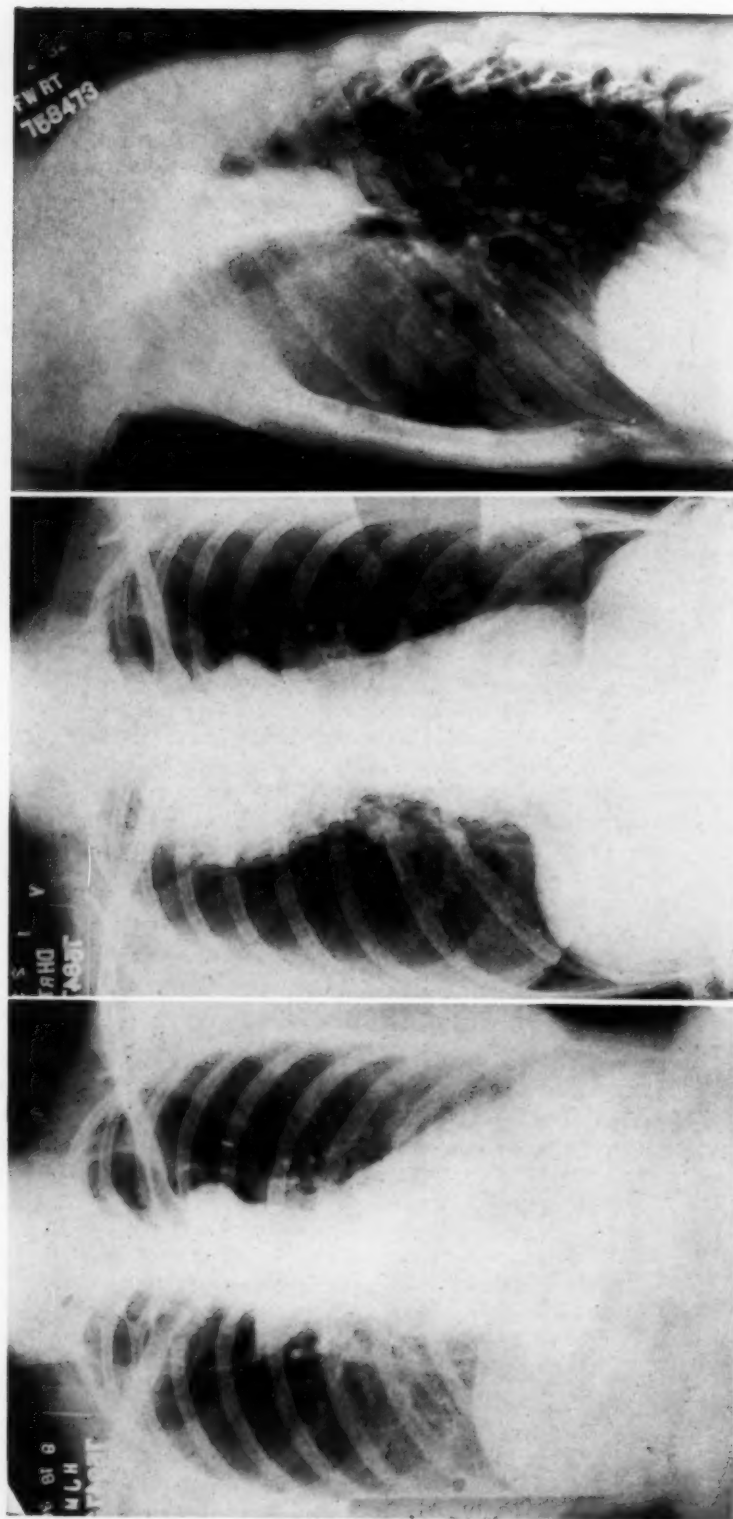


FIG. 1.

FIG. 2.

FIG. 3.

FIG. 1.—Roentgenogram on first admission. Large cystic azygos lobe in right upper portion of thorax. Upper level of fluid between sixth and seventh ribs, posteriorly, and extending across mediastinum to left border of thorax.
 FIG. 2.—Roentgenogram on second admission. Dense tumor in upper, right, posterior portion, corresponding in situation with the position of an azygos lobe.
 FIG. 3.—Lateral view. Dense fusiform shadow in the midst of the upper right portion of the thorax, overlying the shadow of the spinal column. The lower border of the shadow indicates that the tumor communicates with a bronchus at the h.lum.

MEDIASTINAL TUMORS

knife. In several places the cyst had partially ruptured into the adjacent pulmonary tissue; these perforations were repaired by suture. The lower portion of the tumor, close to the hilum, was not adherent to the lung and was covered with visceral pleura similar to that of the lung. The cyst extended across the median line, into the left part of the mediastinum, and then to the left border of the aorta. It was thick-walled, dense, and contained about 750 cubic centimetres of thick, yellowish, pus-like material which contained a great deal of mucus. There was a large bronchial fistula emptying into the

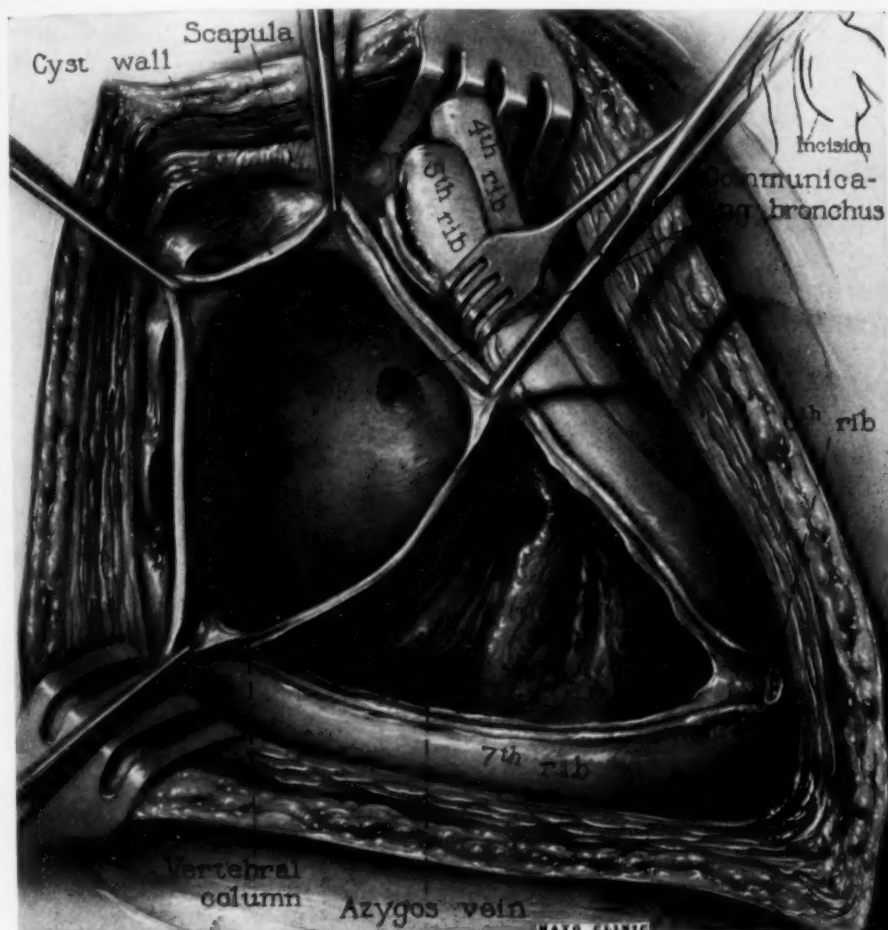


FIG. 4.—Posterior mediastinotomy, with resection of posterior two-thirds of sixth rib, and section of fourth and fifth ribs. Transpleural exposure of cystic azygos lobe in the posterior mediastinum, after it had been dissected free from its attachment to the adjacent lung. The mucoid material of the cyst had been removed, disclosing the large, communicating bronchus in the base of the cyst. The azygos major vein separates the cyst from the adjacent lung.

base, in the middle portion of the cyst. This undoubtedly was the bronchus, through which the material was removed by bronchoscopic examination, and through which the expectorated, pus-like material was flowing. The posterior and left walls of the cyst were fused to the hilum of the lung, and the posterior portion was adherent to the vertebræ as well as to the left pleura and aortic wall. The azygos major vein was markedly dilated, and was incorporated in the wall of the base of the cyst. About two-thirds of the wall of the cyst were excised. The cavity of the cyst was lined with epithelium, and its walls were very vascular and contained remnants of pulmonary

tissue. On examination in the laboratory, the walls of the cyst were found to contain cartilage and all types of pulmonary tissue, indicating that this undoubtedly was a congenital cyst of the lung. The bronchial fistula was closed by suture, and the remaining portion of the sac was sutured over the bronchial fistula, after the lining of the sac had been obliterated. It was necessary to repair by suture three areas in the upper, median portion of the right lung, where the tumor had infiltrated into the pulmonary tissue. The right pleural cavity was completely closed without drainage.

Pathological examination of the wall of the cyst disclosed that it was lined with ciliated, columnar epithelium, and that there were other bronchogenic structures in the thickened portion of the wall, at the base of the cyst.

The patient withstood the operation very well. There was a moderate reaction. Temperature was 101° F. and the pulse-rate was 110 on the second day. The pulse-rate gradually dropped to normal on the sixth day, but on this day there was gradual increase in temperature and pulse-rate. Examination of the thorax revealed a pleural

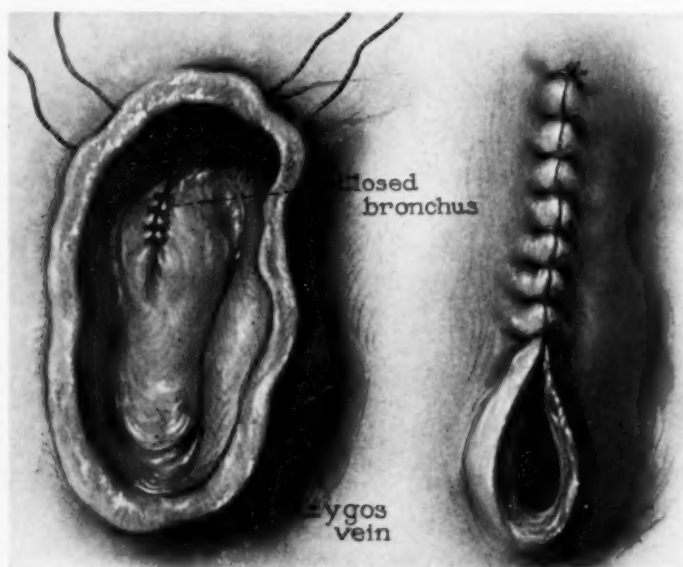


FIG. 5.—Method of closure of a large communicating bronchus with mattress and interrupted sutures of chromic catgut, and also the method of obliteration of the base of the cyst after the ciliated epithelial lining had been completely removed. The lower end of the communicating aperture is left open for drainage.

effusion. About 1,000 cubic centimetres of bloody fluid were removed on one occasion, and found negative to culture. No further aspirations were necessary. The lung remained fully expanded after the pleurocentesis. (Figs. 6 and 7.) The wound healed by primary union. The patient was dismissed from the hospital on the thirty-fourth day, and from my care on the thirty-eighth day after operation.

Comment.—This case is of clinical and surgical interest because of the infrequency of occurrence of single congenital cysts of the lung which do not present symptoms until middle life. The onset of symptoms following a respiratory infection indicated an inflammatory type of lesion, and the persistence of symptoms of infection after the onset indicated inadequate drainage of the cyst. Bronchoscopic examination and aspiration were of little value because of the inaccessibility and tortuous course of the com-

MEDIASTINAL TUMORS

municating bronchus. None of the lipiodol injected into this bronchus reached the cavity of the cyst because, although 300 cubic centimetres of pus-like material were removed by aspiration, the cyst was only partially drained. The cyst was easily accessible through the posterior mediastinal approach; it was markedly distended from the enormous pressure of the contained mucoid material. It had partially ruptured into the adjacent lung in several places. Adhesions between the cyst and this portion of the lung were so firm, and the cyst had penetrated into the substance of the lung so deeply, that it was opened in the course of dissection from the lung. The cyst was so tense with the mucoid, pus-like material, that the right pleural cavity was partially contaminated with its content. This was washed out

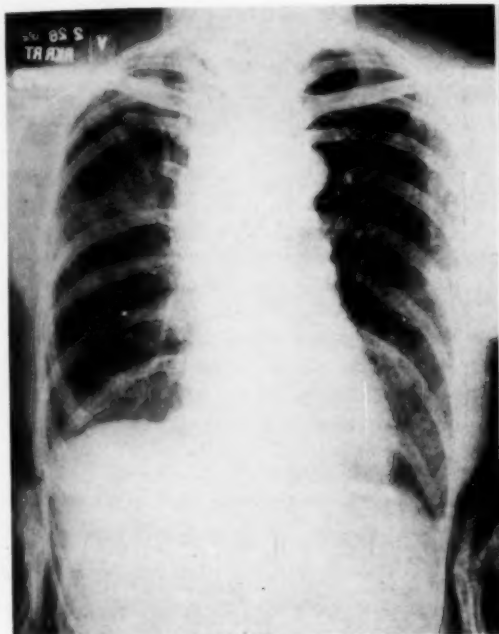


FIG. 6.



FIG. 7.

FIG. 6.—Roentgenogram on dismissal, thirty-four days after operation; the lung is fully expanded.
FIG. 7.—Appearance of the patient, thirty-four days after operation, illustrating the postero-lateral paracapsular incision of posterior mediastinotomy. The wound is entirely healed. Function of the arm was good.

with physiological sodium chloride solution, and there was no resulting infection of the pleural cavity.

The most important surgical problems were removal of the cyst with minimal injury to the adjacent lung, and treatment of the bronchial fistula and base of the cyst. The base of the cyst was firmly adherent to the vertebra and aorta posteriorly, and the inferior portion of the cyst communicated with and was incorporated into the lung at the hilum. The large dilated azygos major vein passed between the cyst and the hilum of the lung, and was fused with the wall of the cyst beneath a pleural fold. There were many large vessels in the base of the cyst, which were ligated with mattress sutures.

After the communicating bronchus had been closed, and the greater portion of the cyst had been removed, the lining was removed from the remaining base of the cyst, and the walls were approximated so as completely to obliterate the remaining space, and to aid in sealing off of the bronchus. This proved to be satisfactorily accomplished, for there was no pneumothorax after operation, and although there was considerable pleural irritation, as evidenced by the extensive, bloody, pleural effusion, only one aspiration was necessary, after which the lung remained fully expanded. Complete closure of the thorax, without drainage, contributed a great deal toward absence of serious immediate or delayed post-operative complications, and to rapid, complete recovery.

DISCUSSION.—DR. HOWARD LILIENTHAL (New York City) said as to the approach used by Doctor Harrington that it is a modification of the one which Doctor Lilienthal had devised himself, modeled on the approach of Enderlen, except that Enderlen used to remove a big flap of ribs and made a truly gigantic, troublesome operation on the chest-wall. Doctor Harrington very rarely even divided a rib. He went in between the ribs and it is astonishing to see how extensive the exposure can, in this manner, be made. One can work in the chest with both hands and see exactly what he is doing.

Another point to make is this: That if a rib has been excised—a long piece of rib—it is not always easy to close the pleura after the operation. If one has made a long intercostal incision and has supplemented it by the division of ribs, usually posteriorly, then when it comes time to close the wound by pericostal sutures, one can put the ribs closer than they were in the normal chest; besides, the pleura can be lifted up between the ribs and its edges everted, the ribs crowding the surfaces together.

The author has mentioned malignant degeneration of some of these tumors. Serious attention should be called to the fact that this can happen and that patients with mediastinal tumors—any tumor of the chest, as far as that goes—ought to be operated upon. He had had great trouble in gaining consent in a good many of his cases, until the patient has been suffering from subjective distress of considerable degree. Valuable time has thus been lost. Certainly if one is going to do anything with a tumor which is malignant it must be early, and if you would do something to a tumor which will undoubtedly make trouble, either because of its size or its malignancy, the sooner that tumor is tackled, the safer will be the operation. Some of those cases that Doctor Harrington treated radically are little short of miraculous. I might have been tempted to marsupialize one or two of these. I have succeeded by a comparatively minor operation in doing this and have had the patient remain well for many years without recurrence.

One can find out whether a case is malignant or not by performing an exploratory operation, and one will, in rare cases, perhaps, be astonished to find that a patient whose case seemed hopeless will get well.

THE CANCER PROBLEM IN THE GENERAL HOSPITAL

BY HAROLD L. FOSS, M.D.

OF DANVILLE, PA.

THE modern surgeon is finding the treatment of malignant neoplastic disease one of his most important and most difficult problems. Contending with an extraordinary surgical condition, meeting unsurmountable obstacles at every step and confronting disheartening results, he finds that, although methods of diagnosis and treatment have improved tremendously, there is still an appalling number of patients suffering from the disease in a stage so advanced that the outlook is completely and thoroughly hopeless. The rapid increase in its incidence, the invariable progressiveness of its course, and, with few exceptions, the ultimate fatal termination combined with absolute failure to discover its cause, render cancer not only the most important, but the most discouraging, of the innumerable problems with which medical science is beset.

In the hospital with which I am connected (Geisinger Memorial) the surgical staff has been greatly impressed with the ever-increasing number of cancer patients admitted to its service, with the advanced nature of the process by the time the patients reach us and, in the majority of instances, with the futility of our treatment. A large number of our beds are occupied by patients suffering from cancer, while much of our time is devoted to the examination of these patients or in apprising anxious relatives of the unpromising outlook. Furthermore, long operating lists are often largely made up of procedures performed in an attempt to cure or, at least, to alleviate the ravages of malignant disease. Such a state of affairs is to be expected in institutions devoted exclusively to the handling of cancer, but the ever-increasing magnitude of the problem must be obvious to all those connected with our general hospitals.

In this connection the relative incidence of cancer to other forms of disease among the general admissions in some of our larger hospitals is a matter of interest. At Bellevue, with 63,000 annual admissions, 1.6 per cent. of the patients have cancer. At the Massachusetts General, with 7,436 admissions, 7.4 per cent. of the patients suffer from malignant disease; at the Pennsylvania Hospital, 2.01 per cent.; at the Henry Ford, 3.1 per cent.; at the Barnes, 4.9 per cent.; at the Jefferson, 4.04 per cent. I was, therefore, led to review our own records with the object of determining the ratio of cancer to surgical admissions in general especially in rural United States; what fluctuations this ratio has shown; what types of tumors were represented; what organs affected; and what progress, if any, is being made in coping with the situation. It seemed to me that such a study might reveal

certain facts, representing possibly the relative incidence of the various pathological types more accurately than a similar study based upon the records of a large urban hospital, noted for its study of special forms of human affliction.

Although it is situated in a small community, the hospital with which I am associated is something of a medical centre for a large rural section, drawing its patients last year from over 400 towns and cities; hence, its patients represent a fairly typical cross-section of those seeking hospitalization.

During the past fifteen years there were admitted to my service 19,707 surgical house patients and of these 7.5 per cent. suffered from some form of malignant disease. When the entire series of 1,478 cases of malignant tumors was studied, it was found that, in the order of frequency of occurrence, the parts affected were as follows:

Breast	190	Penis	7
Stomach	180	Vaginal wall	6
Cervix	159	Larynx	6
Ovary	77	Spinal cord	6
Rectum	72	Pleura	5
Uterus	63	Maxilla	5
Pancreas	63	Scalp	4
Brain	56	Bile duct	4
Face	53	Testicle	4
Prostate	51	Rib	4
Bladder	43	Ileum	3
Liver	40	Ilium	3
Sigmoid	36	Sacrum	3
Colon	36	Tonsils	3
Lip	32	Antrum	3
Esophagus	23	Orbit	3
General abdominal	22	Parotid gland	3
Skin other than face	28	Abdominal wall	2
Mouth	19	Chest wall	2
Neck	17	Tibia	2
Thyroid	16	Rectovaginal septum	1
Mandible	15	Thymus	1
Kidney	13	Optic tract	1
Tongue	12	Retropharyngeal	1
Mediastinum	11	Spleen	1
Vulva	10	Jejunum	1
Lung	10	Perineum	1
Retroperitoneal	9	Humerus	1
Femur	8	Peritoneum	1
Cæcum	8	Omentum	1
Gall-bladder	8	Eyeball	1
Rectosigmoid	8	Multiple melanoma	1

The neoplasms, according to pathological classification, occurred in the following order of frequency:

CANCER PROBLEMS IN THE GENERAL HOSPITAL

Carcinoma	1,158	Endothelioma	13
Epithelioma	149	Hypernephroma	7
Sarcoma	79	Mixed tumor parotid gland	2
Brain and cord tumors (gliomas, etc.)	62	Miscellaneous	9

In view of the widespread propaganda for the early recognition and treatment of cancer and in view of the enormous amount of information on the subject imparted to the laymen, all of which has tended to make the human race cancer-conscious to a degree heretofore hardly conceived of, I was interested in determining what results were being obtained as reflected in the elapsed time between the onset of symptoms and admission to the hospital. This factor is enlightening; yet in the face of the great educational effort that has been put forth the result is neither highly gratifying to the profession nor especially encouraging to those groups and agencies who are devoting their lives to this exceedingly important phase of human welfare.

Each year, in this country, over 125,000 die from cancer, and while it is well known that far more can be accomplished now than was possible a few years ago, nothing approaching adequate treatment has been provided for all these patients, a fact that applies particularly to those living in the rural sections. While in a few centres patients are scientifically handled, thousands are going untreated, or very inadequately treated, largely due to the amazing lack of facilities connected with the only source of relief to which the cancer sufferer has recourse—the average modern hospital.

For example, in Pennsylvania, an enlightened state, with the oldest medical school and the oldest hospital in America, in a state in which the death rate for cancer has almost doubled in twenty years, in which the deaths from cancer last year totalled over 9,000, and in which the number of living cancer sufferers is estimated at about 100,000, from a questionnaire sent to the superintendents of thirty-nine Pennsylvania institutions of over 100-bed capacity situated outside of the cities of Philadelphia and Pittsburgh, I find that only 46 per cent. have radium, that less than 50 per cent. have deep-therapy apparatus, and that only 30 per cent. have any sort of a tumor clinic. In Pennsylvania, 70 per cent. of the cancer deaths occur in people who have not been in a hospital, while 15 per cent. of the abdominal cases, according to Appel,¹ have never had the advantages of an X-ray examination.

In an attempt to determine the degree of adequacy of treatment afforded the cancer sufferer in our rural sections, the annoying, but informing, questionnaire was employed, a study being made of the entire state of Pennsylvania, exclusive of the cities of Philadelphia and Pittsburgh. Answers were received from forty-seven county medical society secretaries. A summary showed that in 64 per cent. of the counties no one trained in the use of deep X-ray therapy was available and that in 42 per cent. there was no one skilled in the use of, or possessing, a supply of radium. About one-third reported that patients were inadequately treated; although nearly all

stated that patients were coming for examination much earlier than formerly. Blame for any delay was placed about equally upon the patient and the family physician. Patients especially lacking adequate care were reported as those in the gastro-intestinal group and those in the need of radium and X-ray irradiation.

Similar data were furnished by 170 surgeons scattered throughout the state, outside of the two largest cities. Of this group, 17 per cent. reported possessing a limited supply of radium, although 59 per cent. reported having it available in one form or another. Twenty-seven per cent. reported that deep X-ray therapy was not available in their respective towns. One-third stated that, in their regions, treatment was quite inadequate; yet over 90 per cent. stated that patients were reporting much more promptly than heretofore.

The greatest needs at present were reported as being:

- (1) More perfect coöperation between the family physician and the man trained in cancer therapy.
- (2) More men skilled in the diagnosis and treatment of neoplastic disease.
- (3) Larger supplies of radium and more deep X-ray equipment, with men competent to apply these agencies.
- (4) Tumor clinics to which the practitioner can refer his patients with some assurance that they will be properly handled.

Patients most in need of more adequate care were reported as being those suffering from carcinoma of the cervix, of the breast, and of the gastro-intestinal tract.

This information, which may be considered fairly accurate, casts considerable light on conditions in rural Pennsylvania, and may be taken as indicative of conditions throughout rural United States. That much must yet be done before anything like sufficient care is provided these patients who suffer from a condition which, next to heart disease, is accounting for more deaths in the United States than any other affliction, is perfectly apparent. While there is an obvious need for more irradiation facilities, it must be emphasized that mere acquisition of the physical equipment is, perhaps, worse than useless, unless it is placed in the hands of those who have received the proper technical training in its application.

Our large city hospitals are well equipped to care for cancer patients. Indeed, certain hospitals are devoted exclusively to their care. However, the institutions in the smaller cities and towns admit the unfortunate carcinoma patient along with other general cases, tolerating them, viewing them with misgiving and a sense of fatalism, and accomplishing little or nothing, chiefly because of the lack of diagnostic and other facilities and because of a paucity of men adequately trained in cancer therapeutics.

The death rate from cancer in the United States per 100,000 of population has shown an increase of from sixty-three in 1900 to ninety-six in 1929,

CANCER PROBLEMS IN THE GENERAL HOSPITAL

an increase of 52 per cent. In 1900, cancer ranked sixth as a principal cause of death in the United States; in 1930, second. There has been a marked increase in Albany; Atlantic City; Lincoln, Nebraska; Newport, Rhode Island; Portland, Oregon; Charleston, South Carolina; and Topeka, Kansas; yet, in contrast, a pronounced decrease, for which there is no adequate explanation, in Canton, Ohio; Erie, Pennsylvania; Kansas City, Missouri; Springfield, Illinois; Trenton, New Jersey; Tampa, Florida; and Utica, New York. (Hoffman.²)

In England and Wales, from which countries we have a very careful analysis of carcinoma mortality and the results of which are in close conformity with those secured from our American records, it has recently been shown that while there has been a pronounced increase in the incidence of carcinoma of the mouth, œsophagus, stomach, gall-bladder, rectum, breast, lungs, pancreas, bladder, and prostate, there has, at the same time, been a corresponding decrease in the incidence of carcinoma of the lip, tongue, jaw, liver, penis, and uterus. To what extent the variations are due to faulty statistical returns, about which there always may be some justifiable skepticism, or to local causative factors, habits, diets, occupations, and other environmental factors, is difficult to determine.

A recent development in the modern hospital is the tumor clinic, to which patients with malignant disease are admitted and wherein they are given special attention as to diagnosis and plan of therapy by a group of men who meet periodically for the sole purpose of furnishing the best modern medical science can provide. Such clinics are, however, to be found only in the larger centres, and probably do not reach more than 25 per cent. of the great army of patients stricken annually with cancer. The other 75 per cent. turn to our small general hospitals, which, in many instances, are far less adequately equipped than those of "up state" Pennsylvania, with the only results that can be expected where no form of treatment, other than certain inadequate surgery, is provided. While it is true that there are in the United States over 1,500 approved hospitals; yet less than one-third—to be exact, 516—have deep X-ray therapy equipment; less than 400 possess any radium, while but forty-four of the 1,579 have a supply exceeding 300 milligrams. New York, as would be expected, has the largest amount—approximately 24,000 milligrams—and Pennsylvania the next, with 10,386 milligrams. In a recent survey, yet uncompleted, made by the Bureau of Mines, it was found that seven states had no radium whatever in their hospitals and that in three states no radium whatsoever is owned. In our cities, especially those with cancer institutions and research laboratories, the supply is liberal—seventeen such institutions each own 1,000 milligrams or more. Of the forty diagnostic clinics especially concerned with the cancer problem the majority are in Massachusetts and New York City. We read of the recent additional supplies of radium furnished certain centres; the five grams recently acquired by the State Institute for Study of Malignant Diseases of New York; of the two grams added to the supply of the Jeannes Hospital in Philadelphia; of

the additional four grams secured by the Department of Hospitals of the City of New York, *etc.*, but these added facilities are of no aid to the horde of sufferers in the rural sections.

A phase of the question of the treatment of malignant disease often accounting for the physician's failure to seek adequate care for his patient is a frequent lack of unanimity as to the best procedure, even when the patient has come before a group of men of the highest training and broadest experience. Attendance at a tumor conference conducted by the member of the staff of some of our hospitals exclusively devoted to the treatment of malignant tumors will quickly reveal that such a lack regularly exists. That most diametrically opposed views are held by men of equally comprehensive experience is constantly revealed in the writings of our colleagues. Within the year two distinguished members of this association have made valuable contributions to the subject of carcinoma of the breast, one holding that irradiation is completely useless as an adjunct in the treatment of this affliction; the other, with equally convincing evidence to support his conclusions, that irradiation is of the utmost value and that only the patient who has received both pre-operative and post-operative irradiation has been afforded the best that modern treatment affords. Recently I listened to a vigorous argument between two men of international reputation on the question of treatment of primary melanoma. One strongly advocated irradiation; the other, only operation. While the majority hold that irradiation is an incomparably valuable aid, a few investigators have advanced the hypothesis that it is accounting for an increasing incidence of metastasis and should be used with much greater caution—perhaps, in certain incidences, not at all. The overwhelming difficulties with which we are surrounded in handling these complex problems render differences of opinion not unexpected, but when experts disagree, then it is no wonder that the practitioner to whom is entrusted the preliminary care of probably 90 per cent. of the patients who are stricken with cancer, with the all too meagre laboratory and therapeutic facilities at his disposal and thoroughly disheartened by past experiences, literally throws up his hands when approached by the patient, or, as a sop to the patient or the harassed relatives, resorts to some form of thoroughly inadequate, often meddlesome, and usually completely futile treatment. As Cox³ has stated: "The average physician lives in the average community. He sends his patients to the average hospital which lacks facilities and equipment. The results are necessarily discouraging. The experiences encountered offer little to the average doctor to build a faith in the possible control of cancer and the results in the rural sections are the same, practically, as they were twenty-five years ago."

If our modern civilization lacks one outstanding need, it is for more adequate provision for the cancer sufferer—not so much in the cities, for there the deficiency is not apparent, but throughout the rural sections, wherein a countless number of these unfortunate humans are the victims of unnecessary and immeasurable suffering. Such a state of affairs will continue to exist,

CANCER PROBLEMS IN THE GENERAL HOSPITAL

probably increase in magnitude, until a sufficient number of centres adequately equipped with laboratory, surgical, and radiotherapeutic facilities to which every cancer patient may have ready access is established.

And so cancer is the greatest public health problem with which we are faced and is one, so far as its treatment is concerned, which the surgeon especially is expected to solve. The most important phase of the question, next to determining the chief etiological factor, is that of the treatment of the rural patients who constitute, by far, the largest group of those afflicted. Whether the solution will depend on the establishment of State- or federal-directed cancer centres, a trend toward which the profession is largely opposed, or to the establishment of adequately staffed and equipped tumor clinics in every hospital in the land, or to some other solution, the responsibility will continue to rest with the surgeon. The next decade should and, I trust, will be chiefly remembered for the profession's successful and adequate handling of the problem of the proper care of the cancer sufferer not only in the city but in the great rural sections of the United States in which the majority of these unfortunate patients are to be found.

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TEMPORARY BILATERAL ABDUCTOR PARALYSIS WITHOUT NERVE INJURY AND TETANY FOLLOWING THYROIDECTOMY

BY HERBERT A. BRUCE, M.D., F.R.C.S. ENG.

OF TORONTO, CANADA

IT WOULD be difficult to conceive a more distressing event following an operation than bilateral abductor paralysis with its accompanying dyspnoea, alarming alike to the patient and only slightly less so to the surgeon, who has the responsibility of devising a speedy measure of relief.

The case that I am about to report is the first that I have had in an experience of thirty years of thyroid surgery, enabling me to appreciate the force of Crile's apt dictum that unilateral abductor paralysis is unfortunate, but that bilateral abductor paralysis is a tragedy.

In Billroth's clinic, a little more than half a century ago, post-operative tetany and injuries to the recurrent laryngeal nerve were very common. In thirty-one cases he reported 30 per cent. of nerve injuries. Von Mikulicz,¹ who was his pupil, observed the frequent sequelæ of recurrent nerve injury, of tetany and cachexia strumi priva, considered at the time to be largely due to rough handling of the tissues and injury of the thyroid nerves, and also that the unilateral operation did not relieve the compression of the trachea when present, which condition necessitated the removal of the opposite lobe, and to obviate these unpleasant complications he devised his operation of bilateral resection—the so-called melon schnitt lobectomy, leaving only that portion of each lobe which is in relation with the posterior capsule and the inferior thyroid artery. He ligated the superior thyroid arteries and the superficial branches of the inferior thyroid arteries, freed the anterior and lateral surfaces of the trachea, and split the lobe longitudinally, removing the melon-shaped section and leaving that portion of the gland and its capsule in the groove between the trachea and the oesophagus, and avoided dissecting too far posteriorly for fear of injuring the recurrent nerve. This bilateral partial resection marked a decided advance in technic and eliminated the complications which had previously been too common. With unessential modification this procedure has been universally adopted.

In my case, however, there was no injury to the nerves, as was shown by the fact that the patient could speak and breathe normally following the operation. She was forty-three years of age, and thyroidectomy was performed for a very large adenomatous goitre involving both lobes about equally, which had caused frequent attacks of dyspnoea and loss of voice. Both lobes were removed under novocaine infiltration supplemented by gas and oxygen, there being no exceptional difficulty met with at the operation. Care was taken to leave a layer of thyroid substance in front of the posterior capsule and on the inner side. After the removal of each lobe the anterior capsule was stitched together. Her voice was normal and there was no disturbance in breathing until thirty-six hours after the operation when it became noisy and labored, and an examination by Dr. Geoffrey Boyd showed both cords fixed in a position of adduction. Oxygen and

TEMPORARY LARYNGEAL PARALYSIS AFTER THYROIDECTOMY

steam inhalations were used, but the dyspnoea increased with great stridor and cyanosis until twenty-four hours later it became alarming and a tracheotomy had to be performed. This gave immediate relief but the next day acute tetany developed. For this we gave calcium intravenously and parathyroid extract, but got no relief until we secured Collip's "Parathormone," and in twenty minutes after an injection of one cubic centimetre her symptoms disappeared. This was repeated daily for one week. The tracheotomy tube was left in for two weeks, when a laryngoscopic examination showed the cords to be moving slightly, and in six weeks' time she began to speak, and at the end of three months she had completely recovered her voice and seemed in normal health.

Wood² records five cases among 425 thyroidectomies at the Bristol General Hospital during the last seventeen years. Each case was operated on by a different surgeon.

Greene,³ reports fifteen cases of temporary paralysis following thyroidectomy and states that it is not infrequently met with, and may occur during the operation from pinching the nerve or stretching it, or from pressure by the finger in controlling bleeding. If the nerve is not cut, the function will be restored usually in a few weeks' time.

Rankin⁴ reports two cases of temporary abductor paralysis in 4,249 thyroidectomies at The Mayo Clinic.

Fowler and Hanson⁵ found in 200 cadavers examined that the posterior capsule of the thyroid gland left the gland at the postero-lateral portion of its lobe and passed directly backwards to the prevertebral fascia, thus leaving the posterior surface of the thyroid lobe uncovered and in direct contact with the nerve.

Nerve paralysis following thyroidectomy may be due to any of the following:

- (1) Œdema or hæmorrhage about the nerves.
- (2) Pull on the nerve (when the goitre is being rolled out).
- (3) A finger behind the upper pole (Crile's view).
- (4) Traction.
- (5) Accidental ligation.

When the paralysis comes on later it may be due to inclusion in scar or malignant tissue. I believe that my case was clearly due to œdema of the tissues surrounding the nerves and compressing them.

It is a fact that the slightest direct or even indirect pressure on the recurrent nerves interferes with nerve conduction and immediately changes the voice. New, Judd and Mann⁶ studied the effect of trauma upon the laryngeal nerves and found that pinching the nerve with a hemostat at various points gave paralysis of the cord. There was complete restoration in every case in thirty to sixty days. That the laryngeal nerves in these cases were not injured was proven by tests of the cord immediately following the operation, and also by the fact that the complication cleared up in the course of six weeks.

It has been urged that in all cases where a thyroidectomy is contemplated, the vocal cords should be examined before operation as a routine, as it has been found in an examination of a large number of persons that about 1 per cent. have unilateral paralysis of the vocal cord. It is advisable that tracheotomy should be done early following thyroidectomy if abductor paralysis develops, because it is not nearly so hazardous a procedure as late tracheotomy, as in the latter case the heart is embarrassed by long labor against congestion.

Although we believe there was no injury to the nerves during operation, and that they suffered subsequently from pressure due to inflammatory

oedema, it might be of interest to recapitulate some points in the procedure which most surgeons now regard as important for the protection of the nerves. After the normal skin incision:

- (1) A vertical incision through the fascia from the level of the larynx down to the sternum.
- (2) Separation of the muscles will now expose the capsule of the gland.
- (3) Division of the capsule on the tracheal side between forceps, working downwards and outwards, taking care to leave a thick covering of thyroid tissue to protect the trachea and larynx. When the posterior capsule is reached, leave a sufficient covering of thyroid tissue to protect the nerve. The posterior part of the thyroid should not be palpated.
- (4) After removal of one lobe get the patient to talk.
- (5) Perfect hemostasis must be secured. Let the patient strain or cough to see if there are any open vessels. Catch individual bleeding points without grabbing a large amount of tissue.
- (6) Avoid rough sponging and pulling.

Now a word about tetany. The parathyroids lie in pairs near the distribution of the inferior thyroid arteries, and are supplied by these vessels. Tetany may be due to crushing by artery forceps or by tying off this blood supply. Halsted, to avoid this, advised ligaturing the branches inside the capsule of the thyroid (which was done in my case). The occurrence of tetany may be also explained as being due to irregular distribution of the parathyroids. Crile⁷ reports five cases of acute post-operative tetany treated by intravenous injection of one cubic centimetre of Collip's "Parathormone," three doses of two cubic centimetres resulting in complete recovery.

A chronic form of tetany, due to destruction of the parathyroids by scar tissue, may occur, in which case there is a long interval after operation before tetany sets in. The onset may be from twelve hours to four months. There are two stages in the symptoms. The most acute phase, with spasms of the limbs, is obvious. The elbows and wrists are flexed and the hand pronated. The thumb is opposed to the palm, the knuckle-joints are flexed and the other finger-joints are extended, the feet and toes being in plantar flexion. Severe pain is complained of. In the alternative phase there is no pain.

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RESULTS OBTAINED IN THE TREATMENT OF RAYNAUD'S DISEASE BY SYMPATHETIC NEURECTOMY AND IN THROMBO-ANGIITIS OBLITERANS BY DESENSITIZATION OF PERIPHERAL SENSORY NERVES

BY ARTHUR W. ALLEN, M.D.

OF BOSTON, MASS.

FROM THE PERIPHERAL VASCULAR CLINIC OF THE MASSACHUSETTS GENERAL HOSPITAL

DURING the three-and-one-half-year period from December 1, 1928, to May 1, 1932, the peripheral vascular diseases at the Massachusetts General Hospital have been cared for under a special assignment. Four hundred and thirty-five of these cases, exclusive of varicose-vein patients, have applied to us for treatment. Of these, eighty-eight have been classified as thrombo-angiitis obliterans and eighty-eight as vasomotor imbalance. The remaining number fall into the groups of arteriosclerotic obliterative disease, senile or diabetic, and diabetes with infection. All of these patients have had the benefit of the general management of peripheral vascular lesions used in our clinic and previously reported. Two hundred and twenty-five of the cases applying for treatment have been sufficiently mild in character for ambulatory care and these have been treated in the out-patient department. Two hundred and ten required and accepted hospitalization. Inasmuch as we have been particularly interested in sympathetic neurectomy in severe and advanced cases of vasomotor imbalance and in desensitization of peripheral sensory nerves in thrombo-angiitis obliterans with painful lesions, it seems in order to report our results on patients so treated.

Vasomotor imbalance.—These cases fall into two main groups, those with apparently primary vasomotor disturbances and range in severity from mild multiple phase-color reactions with periods of normalcy to those who develop gangrene of the finger-tips or toes. In the other group we have conditions complicating the picture in such a way as to suggest a secondary vasomotor spasm. These may have scleroderma or arthritis or be secondary to peripheral injury or infection.

Although there have been some cases of poliomyelitis with secondary vasomotor spasm operated upon by Dr. W. J. Mixter, these will not be included in this report. All of the cases subjected to sympathetic neurectomy are first blocked with novocaine to determine their vasomotor response. In all of these cases the rise in peripheral surface temperature has been above 15° F. Very rarely has a patient without severe, advanced disease been operated upon. Nearly all had open lesions or were incapacitated from the disease. Various members of the surgical staff associated with the peripheral vascular and neuro-surgical clinics have performed the operations. All of the cases reported here were operated upon at least twelve months ago. All recur-

rences that we have seen have come within a shorter period of time, usually four to eight months. The lumbar sympathectomies have usually been bilateral in one operation. A few of the cervicodorsal operations have been bilateral in one stage, but usually these have been done one side at a time. There has been only one post-operative fatality in the entire group, and was reported before this society in 1930. There have been few post-operative complications, the most annoying that of a transient neuritis following the cervicodorsal operations.

Vasomotor Diseases—Primary—(Raynaud's).—In this group, eleven patients have been subjected to twenty-three sympathetic neurectomies, as follows:

	<i>Patients</i>	Vasomotor influence returned—failures:
Quadrilateral	2	Cervicodorsal—eleven in six patients.
Bilateral cervicodorsal	4	Vasomotor influence did not return from
Bilateral lumbar	2	twelve to forty months:
Unilateral cervicodorsal	3	Cervicodorsal—four in three patients.
	—	Lumbar— eight in four patients.
	11	
	<i>Sides</i>	
Cervicodorsal	15	
Lumbar	8	
	—	
	23	

Vasomotor Disease—Secondary.—In this group, ten patients have been subjected to fourteen sympathetic neurectomies, as follows:

		Cervicodorsal	Lumbar	Return of Vasomotor Spasm	No Return of Vasomotor Control
	<i>Patients</i>	<i>Sides</i>	<i>Sides</i>		
Scleroderma	3	3	0	1	2
Arthritis	3	4	0	0	4
Post-traumatic pain and swelling	1	0	2	0	2
Tubercle of feet	1	0	2	0	2
Fibrosis of fingers following infection	1	2	0	2	0
Spina bifida occulta	1	0	1	0	1
	—	—	—	—	—
Totals	10	9	5	3	11

Combined table of vasomotor disorders operated upon:

	<i>Patients</i>	Cervicodorsal <i>Sides</i>	Recurrences	Relieved
Primary disease	11	15	11	4
		Lumbar Sides		
		8	0	8
		Cervicodorsal Sides		
Secondary disease	10	9	3	6
		Lumbar Sides		
		5	0	5
	—	—	—	—
Totals	21	37	14	23

RAYNAUD'S DISEASE AND THROMBO-ANGIITIS OBLITERANS

It is interesting to note that none of the lumbar ganglionectomies has shown a return of vasomotor influence in the feet. In one of these sides due to anomalous distribution there was failure to completely eliminate sweating over the dorsum of the foot but this was observed immediately after the operation and the condition has remained unchanged. We believe that there are two factors that contribute to the constant results in the lower extremity. Most of these operations were done by surgeons who were more familiar with abdominal surgery and therefore were better able to expose and remove a sufficient portion of the sympathetic chain in this region. The most important factor, however, seems to be that in the lumbar region the ganglia are more widely separated and have fewer communicating rami than in the cervicodorsal region. This makes it possible to obtain a wider break in the lumbar chain.

It is to be noted that a greater number of the cervicodorsal operations were successful in the secondary vasomotor disorders than in the primary group. It seems logical at this time to suggest this fact as supporting Raynaud's original hypothesis of an abnormal central vasomotor control in these cases. Certainly there is a greater tendency on the part of nature to re-establish vasomotor function in true Raynaud's disease than in those in which the imbalance may be secondary to local peripheral irritation. All of the operations on the upper extremity were relieved of all or most of their vasomotor influence for periods of from four to ten months after operation. There are definitely more opportunities in this region to leave behind connecting rami, and to fail to remove a sufficient amount of the chain to permanently break the sympathetic influence. Some of our operations in this region, especially in our earlier cases, were purposely limited to the first and second dorsal ganglia and the communicating trunk. Strangely enough, one of our most striking results was in a severe primary vasomotor disease with gangrene in which the inferior cervical was not removed. In this case there has not been a return of vasomotor influence. All of the cases subjected to cervicodorsal neurectomy for the past year and some prior to this time have had the inferior cervical, first and second dorsal and all communicating rami and trunk removed. We hope this will offer more certain prognosis and that there will be fewer instances of return of vasomotor influence.

Thrombo-angiitis Obliterans.—Severe and advanced cases of thrombo-angiitis obliterans with open painful lesions have been admitted to the hospital for treatment under the direction of the Peripheral Vascular Clinic. All of these cases have had general routine measures in addition to special forms of therapy.

In the three-year period from December 1, 1928, to December 1, 1931, there have been thirty-six of these advanced cases in the hospital. Twenty-nine of these were treated by sensory-nerve desensitization, as advocated by Smithwick and White, of our clinic. Alcohol injection was used in all the posterior tibial nerves and in some of the smaller ones, the small nerves being crushed or cut in the others. All the nerves were seldom done at one

sitting, as it has been found that by spacing the procedure a week apart there is less disturbance to the border-line circulation. It has been necessary to take into account rather frequent anatomical variations and obtain complete comfort before proper dressings could be done and postural-change exercises carried out. Also, the maximum benefit of the usually small vasomotor element was best obtained in the completely desensitized foot. These individuals have had very little difficulty arising from lack of sensation. Great care is exercised to prevent ulceration on pressure points by suitable arch supports of sponge rubber and leather. None of this group has complained very much of paræsthesæ. The nerves have regenerated in from four to twelve months—in the later cases return of sensation has more or less accurately paralleled healing and return of function.

Twelve of the twenty-nine cases have required major amputation, due to spreading gangrene or infection. Of the remaining seventeen cases where healing and return of function have taken place, almost all have lost parts of the toes, but all are left with serviceable feet. From previous experience it is safe to prophesy that some of these favorable results are probably temporary, although many of them have had useful painless extremities from one to three years.

In a series of twenty-one cases of this same severe grade of the disease treated prior to the time of desensitization, the percentage of major amputations was more than twice as great as in the more recent group.

If palliative treatment is worth while at all in this advanced group, we believe desensitization is indicated for the relief of pain alone, and although they are time-consuming, a considerable number of useful extremities are saved.

In a few instances we have attempted to alleviate pain in this group by lumbar sympathetic neurectomy, without success. If this procedure has a place in the treatment of thrombo-angiitis obliterans, it should be used in an earlier stage of the disease and limited to those cases with a high vasomotor index.

RESULTS OF OPERATIVE TREATMENT OF CANCER OF THE BREAST

BY FRANK S. MATHEWS, M.D.

OF NEW YORK, N.Y.

IT is purposed to present in this paper the results of operation on carcinoma of the breast both early and late. The surgical operation has been followed, especially in the later years, by X-ray therapy in an increasing percentage of cases. The wisdom of surgical treatment in the late cases may well be open to question, some preferring to restrict surgery to what are called "operable cases." But when surgical treatment is selected for a portion of the cases only, the statistical value of reports is impaired and it ceases to be possible to compare the series of different operators.*

Cures are spoken of for convenience, there being no time in the cancer patient's life when it may be said that recurrence is no longer a possibility.

The characteristics of the series which seem to make it worthy of presentation are:

First, it is not a selected group.

Second, the follow-up is almost complete.

Third, it is the work of an of an individual rather than a group. This has advantages and disadvantages.

Fourth, a surgical technic has been followed which is uniform throughout the period and has varied only in unimportant details.

Fifth, it is believed that the pathological reports are dependable, in nearly all cases being made by Dr. F. C. Wood and Dr. L. C. Knox, at St. Luke's Hospital.

Sixth, it illustrates a willingness to operate for amelioration of symptoms when it is not for the operator's statistical advantage.

Seventh, no group has been erected for the inclusion of patients who refuse to submit to operation. Operation has at times been postponed but no case is recalled in which operative surgery has been absolutely refused.

Two hundred and twenty-five patients have been operated on during the last nineteen years and with few exceptions at St. Luke's Hospital. Three patients have died from operation. In seven cases the clinical diagnosis has not been confirmed by microscopical examination. Two patients have died

* Lewis and Rienhoff¹ say that of their 950 cases of carcinoma, 7.6 per cent. only were dismissed without operation. Handley² reports seventy-seven operations of which twenty-nine were "frankly palliative." He then computes a 45 per cent. of three- to six-year cures, including a patient who dies of pneumonia, as a non-recurrence. Unless all patients operated on contribute to the statistics, comparison with the statistics of other operators will have slight value for each surgeon will have different views as to what constitutes the "frankly palliative" group.

of carcinoma of the uterus—one of them having it at the same time as an epithelioma of the breast and the second developing a carcinoma of the uterine body from which she died five years after mastectomy without signs of local recurrence. If these patients are eliminated, 213 remain for study.* Thirteen of them, though subjected to operation, are recorded as incomplete operations, this meaning either that the mastectomy was not of the usual extent or did not macroscopically extend beyond the disease. If these were eliminated, the number of cases would be exactly 200. These thirteen very advanced cases have all died within a year and no great gain can be claimed for operation. Moreover, it is considered inadvisable to perform palliative operations if an open wound rather than a closed one is to be left for the remainder of the patient's days.

Mortality.—Halsted was wont to say that though his operation for cancer of the breast seemed extensive and time-consuming, it was accompanied by an almost negligible mortality. This has not always been confirmed in the practice of other surgeons. Mortality rates of from 1 to 12 per cent. have been reported. The three deaths constituting the 1.3 per cent. mortality in this list have been, one from pneumonia, one from delirium tremens on the third day, and one from pulmonary embolus on the twentieth day. The pathological department at St. Luke's Hospital reports a 1.6 per cent. mortality for the hospital in breast cancer. White³ reports from Roosevelt Hospital a mortality of 2.9 per cent. Lane-Clayton,⁴ from eight large British cities, reports a mortality of just under 3 per cent. among 2,006 patients. Lewis and Rienhoff¹ report a mortality of 6.4 per cent. from the service of Johns Hopkins Hospital. A short series of cases has recently been reported with a mortality of 12 per cent.⁵

One would think that, with present-day operative technic, there should be no deaths from shock or hæmorrhage, quite rarely from sepsis, and that any legitimate mortality should result from such unavoidable accidents as embolus, apoplexy, myocarditis, *etc.*

Follow-up.—The follow-up from 1913 to May 1, 1932, shows 133 patients dead, seventy-three living, five living with recurrence, two lost to follow-up after remaining well over five years. The total is 213 patients. On five others there was no follow-up. This accounts for the total carcinomas of the series (218) and gives a follow-up percentage of patients from 1913 to date of ninety-seven. Klingenstein⁶ reports a follow-up on patients of Mt. Sinai Hospital for a period of five years as 75 per cent. Lewis and Rienhoff¹ report a 78 per cent. follow-up from the Johns Hopkins Hospital.

* The material includes one male patient with carcinoma. There are two sarcomas, one in a patient who died shortly of local hæmorrhages; the other with fibrosarcoma has remained well over six years. Two patients have survived pregnancy, one of them living three years and the other five years thereafter. In neither was there a recurrence locally nor in the opposite breast. Contrary to a general impression, the pregnancy seems to have been only an incident in the course of the carcinoma. The recurrence was in the pleura in one case and in the supraclavicular glands in the other.

RESULTS OPERATIONS FOR BREAST CANCER

One occasionally sees attempts to give statistical information based on a follow-up of 50 per cent. or less. It would seem as if such statistics could be of little value for they require some form of manipulation either in the form of assumptions as to those lacking or else consider those followed as though they constituted the entire material.

Operation.—The operation is the Halsted-Meyer one with the modification of extensive skin undermining as suggested by Handley.² The skin incision has varied considerably but in the main has resembled that of Halsted. The sacrifice of skin has been moderate and efforts have been made to close the wound without skin grafting. The undermining of tissues has extended into all directions from the middle line to the margin of the latissimus dorsi muscle. The episternal notch has usually but not invariably been invaded, this depending chiefly on the location of the tumor. After making the incision and bringing the dissection in every direction down to muscle, the Meyers technic has then been invariably followed, dividing the pectorals at their insertions and then proceeding with the dissection from the apex of the axilla downward. This seems the more logical method and probably is accompanied by less bleeding. The attempt has been made to remove the tissue in one piece. Formerly supraclavicular dissection was employed in a number of cases but has been almost wholly abandoned in the belief that very little good is accomplished by it.

Accuracy of Diagnosis.—That the "clinical diagnosis of carcinoma of the breast is seldom wrong"⁷ deserves some modification. In the hands of the general practitioner the statement is far from accurate. In the later cases of carcinoma it closely approaches the truth. But in the earliest cases, those in which we are most deeply interested as surgeons, the clinical diagnosis is far from satisfactory. White⁸ says: "It is our confirmed observation that in the early cases it is very often impossible to make a definite diagnosis before local excision." It is because of the clinical uncertainty that resort to frozen-section diagnosis has very frequently been made. The tumor is first incised or excised for macroscopical and microscopical diagnosis. The wound is closed and the operation proceeded with. From the dissector's standpoint, it seems rather undesirable to remove the entire breast as though for a benign condition and then proceed with a radical mastectomy when the tumor is found to be cancer. The microscopical diagnosis, though not infallible, as shown by slight difference of opinion among pathologists, is many times more accurate than the clinical one. In this series, seven cases have been excluded on which radical mastectomy has been done, the clinical diagnosis of suspected malignancy not being confirmed by the pathological report. As far as the follow-up has been made on these cases, it tends to confirm the accuracy of the pathologist's decision rather than the clinical one in these seven cases.

Lymph-node Involvement.—The involvement of nodes has been recorded in almost every case. In 144 patients they were involved and in sixty-eight not. This gives a percentage of involvement of 67.3. The absence of in-

involvement is possibly our best factor in estimating a favorable prognosis. It was found that whereas 67 per cent. is the involvement for the entire group, in the cases remaining well ten years or more, twenty-three in number, only five had involvement—a percentage of 21.7. This prognostic value is not invariable when applied to the individual case, for some without involvement do conspicuously badly while some with involvement may remain local in their metastases and with or without subsequent local removals live for many years. Of forty-five patients with uninvolved glands operated on over five years ago, twenty-nine lived over five years—a percentage of 64.4.

The following is an analysis of freedom from recurrence over a five-year period in cases that had no axillary involvement as reported from three sources:

	Cases	Cures (%)
Sistrunk and McCarthy (Mayo Clinic) ⁹	86	63
White (The Roosevelt Hospital) ⁹	55	70
Mathews (St. Luke's Hospital).....	45	64.4

Bloodgood¹⁰ rather optimistically states: "The probability of the five-year cure when the glands are not involved varies from 70 to 95 per cent., according to the type of the cancer."

Early Deaths.—One-third of the patients in this series have died within two years of the operation. Of those operated on in the last three years—thirty-six in number—eleven are now dead or living with recurrence—30.4 per cent. Of those operated on within the last five years, sixty-two in number, twenty-five are dead or living with recurrence—40 per cent. Other surgeons call attention to this high early mortality and the propriety of operating in these more advanced cases is naturally called into question. But there are justifications for it. Of the less important is the fact that the patients have some mental relief from the knowledge that their tumor has been removed and that a sloughing sore is removed or prevented. More important is the fact that now and then a patient with what seems an unpromising condition goes on with comparative health for a considerable number of years. Three such cases in this series have lived seven to eleven years. A question of more importance is whether the lives of any considerable number of these late cases are shortened by operation. It is my personal belief that of this large group not surviving the two-year period, the length of life is neither appreciably lengthened or shortened with the exception of those who do not survive the operation.

Death from Intercurrent Disease.—In a series of 138 deaths, only nine patients are reasonably believed to have died from other diseases than cancer—a percentage of 6.5. We find reported hemiplegia, cerebral hemorrhage, cardionephritis and acute indigestion. But of these so reported it is certain that some at the time of death were suffering also from evidences of cancer. It seems, therefore, that no great error is introduced into the statistics by including these patients among those dead from carcinoma and it simplifies the statistical handling. In the preparation of this paper about a dozen cases

RESULTS OPERATIONS FOR BREAST CANCER

which we could not follow by other methods were traced at the Bureau of Vital Statistics. Of several of these, other causes of death were given than carcinoma, though all of them died within two years of operations and hence presumably of cancer. The most amusing illustration of this comes from our own hospital. A patient returned to our medical ward nine months after the carcinoma operation, was diagnosed acute pleurisy, discharged as recovered, and is reported at the Board of Health as having died two months later of pleural carcinoma. In view of the above consideration, no statistical account is taken in this series of patients dying with intercurrent disease and if five-year cures only are concerned, the error must be very slight. Of course, if the patients are followed for ten or fifteen years, the statistical error which would be introduced would increase considerably.

Bilateral Carcinoma.—This subject seems rather mystifying. Thirteen of the patients have been known to have had carcinoma of the opposite breast—a rather larger number than in other series. Lewis and Rienhoff¹ reported it in 4.7 per cent. of their cases. In our 218 cases the percentage is 6, or, if one compares them with the total number of patients with recurrence of carcinoma, it is thirteen bilaterals in 145 patients, or 9 per cent. Seven of the patients are now living. Six have no recurrence on the side of the original tumor or had none up to the time of death. In two cases, toward the end of life, carcinomatous nodules were present all over both sides of the chest.

To consider the late appearance of the second carcinoma as a metastasis, we must assume that at the time of the original operation an embolus had reached the opposite breast for the freedom from recurrence on the primary side has seemed impressive. What the embolus is doing or what is holding it in check for seven, eight or eleven years before its clinical manifestation is hard to understand. Nevertheless, we have no pathological basis for belief that any one of them showed sufficient difference in type of the two growths for the belief that the second breast was involved as a second primary carcinoma. There is no evidence of a particularly free lymphatic connection between the two mammary glands. Nevertheless, in a number of cases the nodule has appeared as a small, discreet one in mammary-gland substance without any nodules in the skin or surrounding tissues. It almost seems as if the mammary tissue might possess a special susceptibility to cancerous emboli. One patient had a recurrence after six and one-half years. The glands were not involved at the primary breast operation nor were they at the second. In two patients seen just before death, the breast, axilla and surrounding skin were filled with metastases, but the region of the primary operation was still clear.

TABLE I
RESULTS OF OPERATION
Ten-Year Cures

96 patients—23 living	23.9%
Of 23, 18 without gland involvement.	

FRANK S. MATHEWS

Five-Year Cures

153 patients—58 living	37.8%
Of 58, 29 without gland involvement.	
Or, deducting 9 incomplete operations	
144 cases—58 living	40.2%

The nine patients deducted to obtain the higher percentage of cures would none of them have been operated on by a surgeon with any idea of cure in mind. Some were operated on with local anaesthesia. One operation occupied twenty minutes and none lived over a year.

TABLE II

Five-Year Cures

	Cases	Cures (%)
Adair (surgery alone)	23	8.7
Lee and Cornell (New York Hospital)	75	15
Klingenstein (Mt. Sinai)	57	23
Moschcowitz, <i>et al.</i> (Mt. Sinai) ¹⁵	89	34
White (Roosevelt Hospital)	157	36
Lee (Surgery and pre- and post-operative irradiation)	41	39
Mathews (Surgery, some X-ray)	153	37.8
	or 144	40.2
Adair (Memorial Hospital) (Primary surgery, irradiation or combinations)	197	46
Lane-Clayton (British cities)*	2,006	37.4

Table II presents results of operation with five-year cures as reported in several New York hospitals and in the main the percentages do not differ widely for different institutions throughout the country. This seems to indicate a fairly uniform average type of patient and that operations are performed about equally well in the different hospitals. For comparison with our own hospitals we have inserted the figures as reported to the Ministry of Health for Great Britain. "It has been obtained from the surgical practice at general hospitals of eight of the largest provincial towns in England and Wales. A large proportion of the hospitals are teaching hospitals and are representative of the best work in the country."⁴ It shows, moreover, that the operative results without radiation are about the same as in this country.

Location of Recurrences.—Under this heading the statistical method has been abandoned and replaced by impressions only, for the reason that in such a large number of cases, especially those with early terminations, the patients have drifted away and evidence as to the first appearance of metastases has been of the hear-say variety. It is extracted from the patient's friends, from the patient's physician—often not too disposed to interest himself in observing the first signs of metastases—and death certificates which have seemed notoriously unreliable as sources of information. Recurrences in the chest, pleura, mediastinum or lung have easily headed the list. Metastases in the opposite breast have already been commented upon.

* Of 420 Johns Hopkins cases, known to have died 18 per cent. lived over five years.

RESULTS OPERATIONS FOR BREAST CANCER

It is interesting to observe that though the axillary nodes are involved in 67 per cent. of the cases, yet we seem conspicuously successful in avoiding axillary metastases. This fact is given special emphasis in Lane-Claypon's statistical report from Great Britain.⁴ Most striking to me has been the observation that patients go to their grave with distant metastases, often living a considerable period with them, yet at the moment of death showing no evidence of recurrence in the scar or immediately underlying tissue. This has been especially interesting in the case of patients whose metastasis appeared first in the opposite breast and has led me to the conclusion that we are not to hope for better results by increasing the magnitude of the operation. We may extend the area of skin removal indefinitely but what is gained when the site of recurrence is in the chest? It is realized that this opinion is not generally shared and operating surgeons are known whose operations consume four to five hours, while the operations here reported have usually been completed within an hour and have not been unusually radical, the clavicular portion of the pectoralis major being preserved and the wound being closed in nearly all cases. The prolongation of operation, as in the cases where it is combined with skin grafting, would seem to lead to a higher operative mortality, as seen in the results of the Johns Hopkins Hospital series. Lewis and Rienhoff¹ devote a considerable part of their efforts to proving that the results of the operations at the Hopkins Hospital with extensive skin removal have been superior to those with closed plastics. Their argument seems to me very considerably vitiated by the fact that their surgeons have in the main abandoned it since 1925.

The spread of the disease from the original focus takes place by permeation or by embolus through lymphatics and possibly blood-vessels; and the result of operation must largely depend upon whether at the moment of operation embolus has occurred beyond the local area. Evidence derived from study of carcinoma in animals has seemed to show that many of the emboli fail to live and take hold in their new situation.

Local recurrences in the skin area or subjacent chest wall probably are next in frequency to thoracic recurrences, but these are seen mostly in the prompt recurrences both general and local in the patients dying within the first two years. When embolic transplants have already occurred at the time of operation to liver, pelvic bones, spine and brain, both surgery and radiation can be of little aid; and a hope for better things in the future must depend on the appearance of some agent to ransack the entire system for cancer-cells. Such agents—so far, gold, lead, hormones and serums—seem to have proved sadly disappointing.

Radiotherapy.—Some years ago Sir Berkeley Moynihan was widely reported as saying that he would never operate on another carcinoma of the breast. At about this time there appeared from his own country a report under the auspices of the Ministry of Health for Great Britain⁴ on the late results of operation in cancer of the breast, in which they call the "crude" survival rate for five-year cases 37.4 per cent. The net survival rate was

40.3 per cent., the latter figure being obtained after deducting those not traced and those dying from other causes than cancer. Similar figures for ten-year cures were 25.2 per cent. crude and 28.5 per cent. net. One wonders what evidence he had that matters could be improved by abandoning the surgical treatment of cancer and resorting to other methods. Probably he had been overinfluenced by discouragements in his own operative material. In the government report just mentioned, it is stated that "data are insufficient for any deduction as to the value of post-operative treatment with X-rays" and "so far as they go they can hardly be claimed as a great success for radiology."

At that time the work of Keynes¹¹ was too recent as applied to operable cases, and still is, to be used as a basis of comparison between results of radium and operative surgery. As regards the X-ray treatment of breast cancer Lee says,⁸ "The majority of cancers of the breast are relatively radio-resistant," "to deliver an efficient dose one must use interstitial irradiation." Lewis and Reinhoff,¹ in their exhaustive study of the operative results of cancer of the breast, devote a part of one sentence to "the very questionable effect of radiation." Pfahler¹² has recently reported his treatment of cancers of the breast, the number of cases being over a thousand, and has employed X-ray almost exclusively. He seems to have no hesitation in treating operable cases by this means alone; but as these cases have not been confirmed by microscopical examination and rest entirely on his clinical impression, the results are hardly to be used for statistical comparison with other series of cases. Adair¹³ says that: "As a general rule mammary cancer is not so radiosensitive nor so efficiently treated by any of the irradiation methods as cancer in certain other organs, such as carcinoma of the cervix and basal-cell epithelioma of the skin," "the occasional case of mammary carcinoma under a few treatments by irradiation completely disappears," "in general we have given up our attempts to treat this disease by external irradiation alone. We usually fail with this although there is an occasional exception. It requires heavy and prolonged irradiation by both interstitial and external methods to hold mammary cancer in abeyance to the point of a five-year cure."

To turn now to the present series of cases, it may be noted that the amount of X-ray used in the earlier cases was very small. As time has gone on a very considerable portion of the patients have received X-ray treatments—usually one treatment before leaving the hospital. After leaving the hospital, some have disappeared after a treatment or two while others have remained under observation in our radiotherapeutic department for four or five years. We are not in a position, then, to draw comparison between cases so treated and those treated by surgery alone. Of twenty-two patients now well and operated on prior to 1923, eight cases had X-ray and fourteen had none. But of the eight patients several only received their X-ray some years after operation. In two or three this was given after a small recurrence. There is little evidence, then, that the X-ray has

RESULTS OPERATIONS FOR BREAST CANCER

contributed anything substantial to these results, though it might be reasoned that the number of such ten-year cures would have been larger if all the patients had received X-ray. Only one patient has suffered any harm from radiation. She has a very distressing X-ray burn. On the other hand, it has only been my fortune to see two patients in whom there was ocular evidence of disappearance of metastases. One of these patients had a fairly encapsulated medullary carcinoma. A year later, to my surprise, there were numerous small nodules in the axillary skin. These disappeared under X-ray and the patient is now well, five years from the time of operation. The other patient had supraclavicular glandular enlargements extending as high as the tonsillar node. In three months these have strikingly subsided, to be replaced by a moderate fibrosis.

The advantages, then, of post-operative radiation with the X-ray as observed in this series are disappearance of metastases, as above, in two cases; relief of pain, at times conspicuous, even though the growth as shown by clinical or X-ray evidence is steadily extending. It is easier to keep these patients under observation for they have the feeling that they are receiving treatment as well as observation. Another considerable advantage of post-operative X-ray is that it has very largely replaced secondary operations, an advantage both to the patient and the surgeon. We feel disposed to advise, or at least present the option of post-operative radiation, even to the early operative cases, the radiation being instituted promptly after operation though having very little evidence that the five- and ten-year cures depend to any considerable extent on radiation. We think of it as an addition to surgery.

It is interesting to compare the results of surgery with little dependence on radiation with the results of treatment at the Memorial Hospital, where every form of radiation, supplanting surgery, pre- and post-operative by X-ray, radium packs, interstitial implantation of seeds, tubes and needles, has been employed. The emphasis of the institution has seemed to be on radiation methods rather than upon surgery. This is an inference drawn from the fact that in the Memorial reports radiation alone on operable cases is more frequently reported than surgery alone; though a combination of the two is more often employed than either method alone. Adair¹³ reports ninety-one five-year cures among 197 patients—a percentage of 46. But this percentage is not based on the entire material available at the hospital but what seems to be a very small fraction of it. He reports 500 cases or more a year as passing through their clinic. The results from surgery alone seem surprisingly poor. There were twenty-three radical mastectomies with two five-year cures—a crude result of 8.7 per cent. cures; or, after deducting four deaths from intercurrent disease, a rate of 10 per cent. is extracted. We are left to conclude that the poor result of surgery may depend on a chance dependence on the smallness of the series, or that they have been unfortunate in the selection of cases.

Lee's¹⁴ best results after five years are recorded for pre-operative irradiation, surgery, and post-operative irradiation combined, the number of cases being forty-one and the percentage of five-year cures 39. All things considered, their results seem no great advertisement for their varying methods of applying irradiation as compared to routine operative surgery in unselected cases.

Impressions which may need revision with time are:

- (1) The cures from cancer of the breast are not proportionate to the time devoted to operation or to the extent of the local mutilation.
- (2) Improvement in results in the future is not to be hoped from making our surgery more radical.
- (3) Irradiation by the different methods at present in use has not demonstrated a replacement value as compared to surgery.
- (4) Cures depend on earlier operation of reasonable extent and even more on a mystical something which pathologists are now exploring and which is spoken of as the biology of the tumor.

A series of 218 unselected cases of carcinoma of the breast have been submitted to operation. In 67 per cent. of these the axillary nodes were involved. In thirteen patients the operation is recorded as incomplete, and in several others supraclavicular glands were involved. 23.9 per cent. of the patients operated on over ten years ago survived the ten-year period and some of these are now living from ten to nineteen years from the date of operation. 37.8 per cent. of a series of patients, which includes a number not usually classed as operable, have passed the five-year period. The results compare favorably with those of well-known operating surgeons and seem quite as good as the results of those who largely replace surgery by irradiation. I have no intent to replace operative surgery in operable cases by any form of radiation, but hope to continue the operative treatment with as much aid from radiation as the methods now in use or to be developed may offer.

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**WHEN SHOULD IRRADIATION WITH RADIUM OR X-RAY
PRECEDE OPERATION OR BE EMPLOYED
WITHOUT OPERATION?**

BY JOSEPH COLT BLOODGOOD, M.D.

OF BALTIMORE, MD.

THIS title was chosen, the paper planned, and much of my evidence accumulated some time in January, 1932, but very shortly after an invitation came to present a paper in Paris on April 26 before the French League Against Cancer on the activities in this country for the control of cancer. As I accepted this invitation I was compelled to drop further study of the material for my paper to be delivered before the American Surgical Association in May. On arriving in London, after ten days' study of the radium problem in Paris, I was so much impressed with the work of London surgeons in their treatment of cancer of the breast and cancer of the mouth and larynx with interstitial needles containing radium salts, that I postponed my return home and cabled the American Surgical Association my inability to present my paper in person. In response to an urgent message from the ANNALS OF SURGERY inquiring about the paper for publication, I am writing a very brief report, but this will include my observations in Paris and London, my wider reading of the literature while abroad and the careful study of the splendid, even remarkable, report of the Royal Commission of the Province of Ontario on the methods of the treatment of the sick with X-rays and radium.

For some years, after a very large experience with sarcoma of bone, I have urged that irradiation with deep X-rays should precede biopsy or any further operation, when the X-rays suggest malignancy. The chief reason for trying irradiation first for sarcoma of bone is that in a certain number of cases cures have been accomplished—not many, but a few, and among these cures are not included the cases of benign giant-cell tumor. The deep X-ray therapy is available all over the country, so there is no difficulty in beginning the treatment at once and in giving the patient the benefit of a full trial while the diagnostic survey and consultation are going on. In one of my own cases in which there was great difference of opinion as to the nature of the disease, even after biopsy, the boy's limb was saved by pushing deep X-ray therapy to its limits. We have not had sufficient experience to state that a four-gram pack offers any more than deep X-ray therapy, but I have records of three cases in which smaller amounts of radium were employed. In one case in which there was no biopsy, the patient is living eleven years after treatment. Then there are two cases in which the biopsy demonstrated that the tumor was a small, round-cell sarcoma of the Ewing type. One of these patients is alive and free from recurrence six years,

IRRADIATION OF CANCER

and the other lived four years without local recurrence, but succumbed to metastasis to the lung. I have discussed this again and again in the literature. The evidence is summarized in two chapters in Geschickter's book on bone tumors published by the American Journal of Cancer.

I repeat and emphasize that, with our knowledge as it is today, it is distinctly best to begin the treatment of every bone lesion which, in the X-ray,



FIG. 1.—Keynes' method of needling cancer of the breast by three radium needles near sternum, following the technic of Sampson Handley of London, who has employed these for ten years after operation. (Godfrey Keynes, in the British Journal of Surgery for February, 1932.)

is suspicious of malignancy, with a thorough and complete course of irradiation.

Cancer of the Breast.—I doubt if we need any more statistical studies to inform us what operation will accomplish in cancer of the breast. No one has improved on Halsted's statistics, which in the beginning dealt with late cases, and as Halsted's five-year cures increased the explanation was not better surgery, but a larger number of cases without metastasis to the glands

in the neck and axilla. Before we excluded border-line tumors from Halsted's statistical studies, the percentage of five-year cures after operations performed by himself or his associates, in which the glands were not involved, was 85. When, in 1915, I excluded the border-line tumors, as recently published in the *American Journal of Cancer*, the figure reduced to 70 per cent. This corresponds pretty closely with the statistical figures in the world's literature today. When the axillary glands are involved, as proved by the microscope, the five-year cures fall to 20 per cent., and the ten-year cures, as recently brought out by Lewis and Rienhoff, to 10 per cent. I had a very large personal experience from the very beginning with post-operative irradiation after operations for cancer of the breast in which the axillary glands were involved. It has been my rule not to use irradiation when the axillary glands are not involved, so it must be distinctly understood that my conclusions are based upon cases in which the chances of a five-year cure are about 20 per cent. after operation only.

I have been unable, in this group of cases, to find out that post-operative irradiation with deep X-rays has increased the five-year cures, or reduced the number of local recurrences, no matter what the explanation. I mean by this local recurrences due to incomplete chest-wall dissection in favorable or unfavorable cases, and local recurrences which are better explained by the extensive local involvement at the time of the operation and which take place no matter how painstaking the chest-wall dissection, or whether this dissection is done by knife, cautery or electric needle. Greenough, of Boston, in his investigations of his own material and of that collected by him as Chairman of the Committee on Cancer of the American College of Surgeons, agrees with my conclusions. Burton J. Lee, in his more recent papers and after his unusual experience, is not satisfied with post-operative irradiation after operations for cancer of the breast, but has substituted pre-operative irradiation and employs radium instead of deep X-rays. In France and England and throughout the world, there has been an immense experience with post-operative irradiation with deep X-rays. Sampson Handley still uses post-operative deep X-ray therapy, and is so modest that he does not realize that his results are due to his surgery and not to diathermy and irradiation. Williams, of St. Thomas' Hospital, in London, has compiled the largest statistics and has made no differentiation between "glands involved" and "glands not involved." I spent some hours with him over his tables. His conclusions agree with mine—there is no increase in the number of five-year cures and no decrease in local recurrences. It is only fair to state that the majority of his patients were in the later stages of cancer of the breast with involved glands, all clinically malignant. I spent an afternoon with Geoffrey Keynes, of St. Bartholomew's Hospital, in London. His most recent paper on the treatment of cancer of the breast by the insertion of radium needles was published in the February, 1932, number of the *British Journal of Surgery*. Doctor Keynes was good enough to send for a large number of his cases and allowed me to examine them with him, and

IRRADIATION OF CANCER

later to study the pathology of the biopsy, or where for some reason the breast had been removed. It is important to remember that in the cases of cancer of the breast treated by Doctor Keynes, the clinical diagnosis of malignancy was positive. In the majority of the patients the disease was late, the skin was adherent or ulcerated, the glands palpable. In spite of this, a large percentage of these patients are living and are clinically well; none are suffering with lymphedema of the arm. They were all happy and free from pain. Now and then, when a breast was secondarily removed because there was still an indurated mass, no cancer was found in the sections. There has been little or no study of the glands with the microscope. The point which impressed me most was this: Here is a method of treatment that promises just as much comfort with much less risk of post-operative complications, especially lymphedema, than an attempt to cure late cancer by the complete operation; and I feel confident that this method of interstitial irradiation or of needling the breast, or some other form of irradiation, will ultimately take its place as a palliative treatment rather than operation for cancer of the breast. At least it can be tried first. This is a method I am now employing when the clinical picture of the malignant tumor of the breast indicates that the chances of a cure by operation are not only small, if any, but the necessary dissection would be done at considerable risk of being followed by that distressing complication, lymphedema of the arm.

My personal experience with pre-operative irradiation is small. In a few of the cases a complete operation has followed. In a larger number, because of definite hopeless signs, no operation has been performed.

If my colleagues think anything of my experience in this matter, I hope they will understand me correctly when I urge them to cease using extensive surgery as a last resort in the treatment of extensive cancer of the breast. Our experience with irradiation with deep X-rays, or radium in its different forms, is sufficient to justify us in using this non-operative treatment, for at least palliation. Incomplete operations for cancer of the breast never cure and often make the patient much more uncomfortable than after no treatment at all.

When one explores a doubtful lump in the breast and finds it malignant, the entire evidence favors the complete operation, or, if the cancer of the breast has been of short duration and is clinically in the earliest stages, there seems to be no objection to giving pre-operative treatment to be followed later by the complete operation. This is, as yet, purely experimental, and at the present moment I am giving preference to operation in all early cases.

In a few years more our colleagues in London will be able to inform us on the results of needling cancer of the breast in its early stages. If their percentage of five-year cures is more than 70 and they have biopsies to prove that the lump was cancer, they will have sufficient evidence to justify the procedure.

Cancer of the Cervix.—I know that a number of my gynæcological col-

leagues in this country still operate on very early cancer of the cervix, a very few give a preliminary treatment with radium. Dr. Victor Bonney, of Middlesex Hospital, still operates and performs a Wertheim. Fortunately, it was my privilege to witness Doctor Bonney perform his operation—a masterpiece of surgical technic. I took the liberty of telling him that if the results of radium treatment were better than his results, no longer would anyone be justified in using surgery for cancer of the cervix. In spite of this the consensus of opinion of the world's authorities favors the treatment of cancer of the cervix with radium combined with deep X-ray therapy in

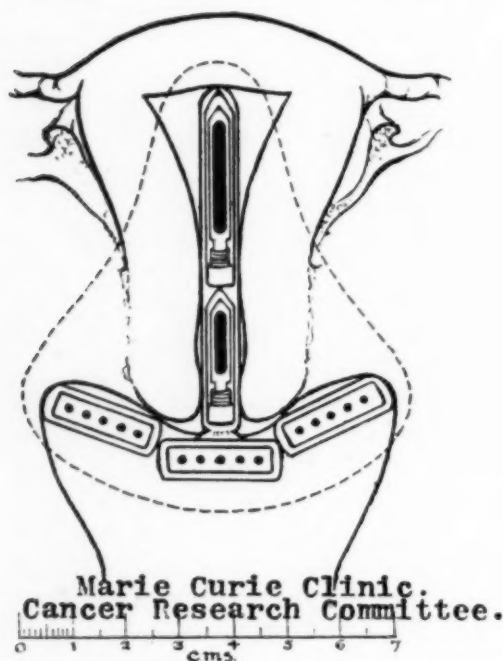


FIG. 2.

FIG. 2.—The dotted line shows the zone of effective radiation with the radium placed in position for the treatment of cancer of the cervix. (Radium Treatment of Cancer of the Uterus; Report of the Cancer Research Committee. H. K. Lewis, Ltd., London, 1929.)

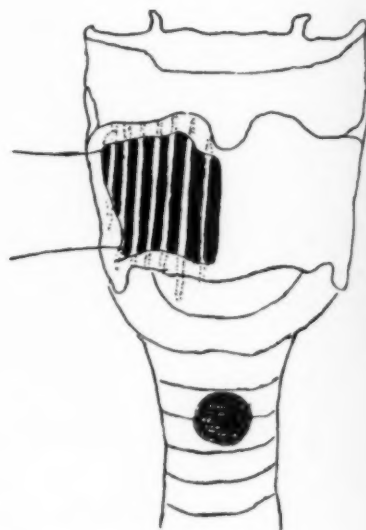


FIG. 3.

FIG. 3.—Harmer method of placing needles into a fenestrum made in the cartilage of the larynx. (Practitioner, January, 1930.)

late cases. The results today in all cases, in the great clinics, are recorded at about from 33 to 35 per cent. of cures at the end of five years, but this cannot be compared with surgical statistics, because radium is employed in all cases, even in the hopeless and inoperable ones, while surgery is employed in only the early cases, or the so-called Group II, as classified by the League of Nations Committee.

My personal opinion is that the evidence favors radium treatment. Even when the cancer of the cervix is discovered by biopsy only, radiation seems to offer just as much as surgery with less risk.

It must be emphatically stated here that the danger of failing to cure a very early case of cancer of the cervix in the hands of an inexperienced

IRRADIATION OF CANCER

and untrained radiologist is just as great, if not greater, than the danger of post-operative death after a Wertheim operation performed by an inexperienced surgeon. The cure of cancer of the cervix depends upon the training of the surgeon and of the radiologist. Unfortunately for women with cancer of the cervix today, we have too many trained operators, and not enough trained radiologists.

Cancer of the Oral Cavity.—Unfortunately the majority of radiologists, whether they are also trained surgeons or not, fail to realize that the earliest stage of cancer in the oral cavity is usually an operable lesion just like the pre-cancerous lesion of the oral cavity, and that it is just as easy to completely remove the visible, palpable spot with a sufficient margin of healthy tissue with the cautery, electric needle, or even, in some areas like the lip,

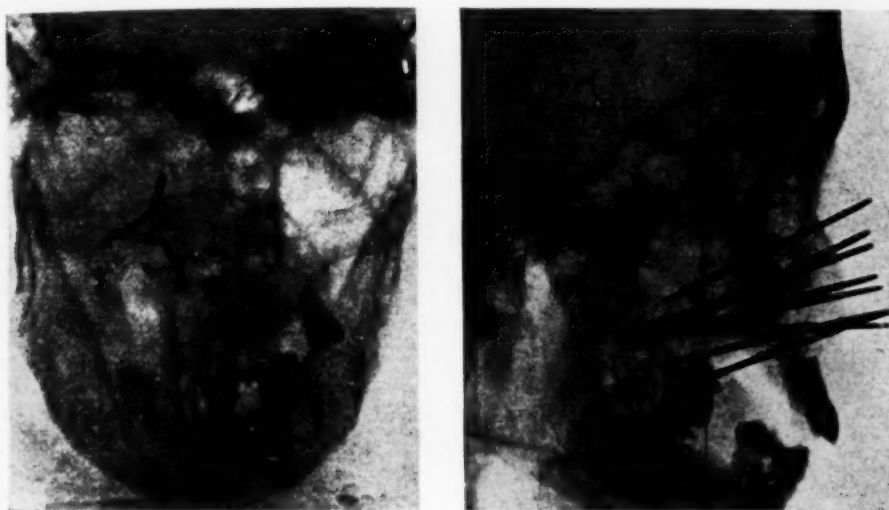


FIG. 4.—Shows method of introducing needles into the antrum for cancer of upper jaw. I examined, with Mr. Harmer, a number of apparently four- and five-year cures after this method. (*Acta Radiologica*, Vol. X.)

with the knife, as to treat it with radium. This complete excision of the small benign or early malignant lesion, properly performed, should accomplish a cure in every case, except in those few cases of cancer in which the glands may be involved.

However, in all cases of cancer of the oral cavity which has extended beyond the possibility of easy operative removal, irradiation with radium is the treatment of choice today. Surgery has accomplished cures in such cases, but always with more discomfort and more mutilation. In spite of my extensive experience over many years with this form of surgery, with knife, cautery and electric needle, I have given it up in favor of irradiation.

I will not take time or space to discuss the different types of irradiation of the oral cavity. We must look upon the introduction of irradiation as a great achievement in the treatment of cancer of the oral cavity. Many cures have been accomplished, whereas, if surgery had been employed, there would

have been greater discomfort, greater mutilation and, perhaps, a smaller percentage of permanent cures. I am speaking now of local cancer without involved glands. When the glands *are* involved, the best chances of a permanent cure depend upon their ultimate complete removal. If the involved glands are metastases from a cancer of the lower lip, the five-year cures are 50 per cent., while when the primary lesion is of the tongue or of the floor of the mouth, the five-year cures are 10 per cent. I am unable to obtain evidence as yet to inform us whether pre- or post-operative irradiation with X-rays or radium increases the number of five-year cures. There is no objection to giving the patient the benefit of both, but there is no question that in those cases in which the complete removal of the glands is possible, operation offers most, and as a rule one must attempt it to find out if the glands can be removed.

Cancer of the Larynx.—I was very much impressed with the results of treatment of cancer of the larynx by Mr. Harmer. It was my good fortune to examine a number of his cases in which the treatment dated back three to five years. The larynx and the cords appeared normal. The patients were clinically well. No glands had been removed and no glands were palpable. I witnessed operations by Mr. Harmer and Mr. Cade. First, there was general anæsthesia with gas-oxygen through an intratracheal tube, most expertly administered. Then, on one or both sides of the larynx, according to the extent of the growth, a piece (fenestrum) was removed from the cartilage, and into this area were placed a sufficient number of needles loaded with radium salts. The method is, of course, simpler than laryngectomy. To me, the results were marvelous, and if the ultimate statistics prove that the results are as good as after laryngectomy, cancer of the larynx will have lost most of its horrors.

Soft-Part Tumors Anywhere.—I have made some contributions to these before, but a brief résumé of the rationale of testing all palpable nodules with X-rays or radium explains best the value of pre-operative irradiation with X-rays or radium. For example, let us take a small nodule near a great nerve trunk—median, ulnar, popliteal, sciatic. In the first place, we know that these nerve-sheath tumors may be multiple. Many of the local recurrences, or recurrences near the scar after the removal of a nerve-sheath tumor, whether benign or malignant, can be explained by leaving behind one or more smaller tumors of the same kind which were not exposed when the larger one was removed. Our records show numerous such examples. Second, irradiation may be followed by the disappearance of the tumor, or after getting smaller it may remain stationary. In a number of instances, rather than resect the involved nerve, we have succeeded in keeping the tumor small and not growing for years under repeated irradiations with X-rays or radium.

Perhaps most important of all, when an apparently small and operable tumor is properly irradiated and does not disappear or show any evidence of becoming smaller, and then the tumor is explored and the operator dem-

IRRADIATION OF CANCER

onstrates that the complete removal means resection of a motor nerve, or of a vessel involving the circulation of a limb, the operator is justified in proceeding with that complete resection. There is no difficulty in getting the exact nature of the tumor. If biopsy proves it to be malignant, there is no choice; if benign, one may attempt to remove all of the growth possible without injury to the nerve or vessel and then depend upon a tendency of the remaining benign tumor to remain quiescent, or be held by post-operative

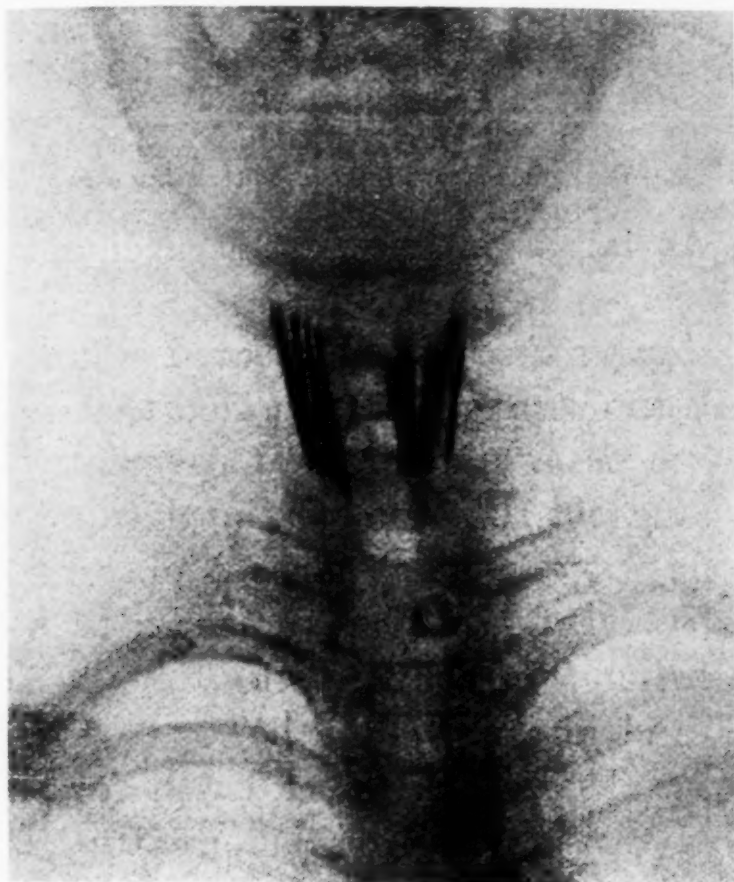


FIG. 5.—X-ray after needling both sides of larynx by Douglas Harmier, surgeon at St. Bartholomew's Hospital, London.

irradiation. In such cases there is no danger of metastasis, but ultimately, because of recurrence, complete resection may have to be performed. The soft-part tumor may be large; its removal may mean amputation or mutilating resection. It may be present within the abdomen or the chest, or involve important structures of the neck. It is far better to give these tumors pre-operative irradiation without preliminary biopsy or exploration, because in many cases the tumor disappears and does not recur. Many of these cases have been held, and held for years, by repeated irradiations.

I am confident that the decision to operate first, or irradiate first, or do a biopsy first, is largely influenced by who sees the patient first. Therefore, the ideal arrangement is for the general practitioner or family physician to refer his patient to a tumor clinic where the patient will come under the diagnostic supervision of a staff rather than an individual. It is also essential that financial considerations should not influence diagnostic and therapeutic procedures. This undoubtedly is less apt to happen in a clinic.

As this paper must be mailed now, it cannot be lengthened. In the larger paper to be published all that can be added will be the evidence on which these somewhat dogmatic statements are made. I urge my surgical colleagues who perhaps have not given the same time or had the same opportunity to investigate the remarkable advances made in the treatment by irradiation with X-rays or radium, to give consideration to irradiation with X-rays or radium by competent radiologists before surgical intervention and often even before biopsy. It can be employed just as the old therapeutic test for syphilis has been employed in the past.

As the number of patients increases whose local lesion is clinically of small extent and who give a history of signs or symptoms of short duration, the chances of curing the lesion, if it is malignant, increase very greatly as, due to the difficulties of diagnosis, microscopical, and the choice of method of treatment of the local lesion, no harm can be done by pre-operative irradiation in the hands of a trained radiologist, but much harm can be done by an unnecessary operation at the hands of the greatest and most expert surgeon.

INOPERABLE AND MALIGNANT TUMORS*

By WILLY MEYER, M.D.

OF NEW YORK

THE principal phases in the evolution of medicine and allied sciences within the last one hundred years have left their lasting imprint on the cancer problem. Naturally pathology was in the lead. The teachings of Theodor Swann, originally of Halle, Germany, later in Liège (Louvain), that cells plus medium had to be considered; the teachings of Carl Rockitsky of Vienna in the '40's, that the humors (or medium) were at the bottom of diseases generally; the teachings of Rudolf Virchow of Berlin in the '50's, erecting the cellular pathology, are reflected in the writings of many authors on cancer up to the present time. The unexplained rôle of a group of cells, suddenly and mysteriously turning into disorderly growth, destroying their neighbors, putting themselves in their place, then slowly but surely undermining the health of their host, are discussed up to this day.

Then came the era of bacteriology founded by Pasteur, Lister, Koch and other schools, beginning in the late '60's, which naturally made medical men who had to treat cancer patients and the scientists of the affiliated branches ponder: cancer, too, must be produced by a living organism. Up to this very time brilliant minds here and abroad cling tenaciously to the infectious theory.

Gradually the advance of organic chemistry brought forth the newest branch of medical science, biology, with its adjuvants: biological chemistry, biological physics, biological physical-chemistry,—a thorough study of the living organism, all of them seconded by physiology, pathology and cancer research.

The treatment of cancer also reflects these various theories of the last one hundred years.

Today we are in the midst of the biological treatment of cancer in coöperation with biological chemistry and biological physics as far as inoperable cancer is concerned.

Operations on operable malignant tumors, of course, remain within the domain of modern cancer surgery. By cancer surgery the tumor "cancer" with all the anatomical groups of regional lymph-nodes are removed and in many instances the patient appears to remain clinically cured. If a biological systemic after-treatment were added in *every* instance, we believe the majority of such patients would remain cured after a properly conducted radical operation.

* This paper, written by Dr. Willy Meyer a few days before he died in February, 1932, had been announced by him to be read before the American Surgical Association Meeting at New Haven in May, 1932, and was read by title.

Personally we have accepted as a good and working hypothesis the assumption that cancer grows only in an alkaline medium and not in an acid medium.

Following this lead, we are trying to change the increased alkalinity of the blood, which was found in every one of the cases of advanced carcinosis studied by us within the last six months, over towards and into the sphere of acid reaction of the blood.

Careful clinical observation and reliable intermittent determination of the pH of the blood of the patient as far as science has advanced in this field today has been our guide.

Biological treatment as practised at the Lenox Hill Hospital at present is principally represented by artificial fever with the help of the large General Electric Corporation "Radiotherm," the inhalation of a mixture of oxygen and carbon dioxide, 94.5:5.5 per cent., deep X-ray therapy, ketogenic diet, intramuscular and intravenous injection of gluconate of calcium, and ammonium benzoate per os.

At this time we believe that, as soon as clinical examination or operation has proved the disease to be beyond the reach of the knife, the biological (acidotic) treatment should set in. In far advanced cases it seems that lacking metabolism balks correction. These patients will die at present.

May we say in conclusion: Those who believe that the so-called inoperable cancer patients should be treated on biological principles seem to be on a possibly correct track. But this big experimental task is neither that of a few men nor of a few hospitals. It is the task of all colleagues who can see a modicum of truth in these assumptions, a possible lead out of the cancer labyrinth. The hospitals and research laboratories of the world should join and help in advancing this big problem as carefully and as rapidly as possible in the interest of suffering humanity.

ULCERATION OF ABERRANT GASTRIC MUCOSA IN MECKEL'S DIVERTICULUM

AS A SOURCE OF INTESTINAL HÆMORRHAGE

BY JAMES M. MASON, M.D.

AND

GEORGE S. GRAHAM, M.D.

OF BIRMINGHAM, ALA.

PRIOR to 1903, intestinal hæmorrhage originating in ulceration of Meckel's diverticulum had not been observed, and not until the report of Deetz,¹ in 1907, had the relation of aberrant gastric mucosa to ulcer of the diverticulum been considered. The acceptance of peptic ulcer of Meckel's diverticulum as a definite clinical entity and the importance of intestinal hæmorrhage as a symptom thereof has resulted from a careful study of an increasing number of cases which are found to present a uniformity of symptoms and histological findings. Much of the evidence is very recent. Between 1903 and 1922, seven cases of intestinal hæmorrhage from ulcer of Meckel's diverticulum were reported at irregular intervals. This paper is based on a consideration of these cases and of twenty-six others, including one of my own, which have been reported since 1924, and the number is now sufficiently large for one to draw conclusions. The disease is one of infancy and childhood. In only one of the adult cases reported does the history fail to go back to childhood as the starting point of intestinal bleeding; and in that instance the patient, aged forty-one years, had suffered since the age of seventeen with digestive disturbance, and for eleven years with recurring intestinal hæmorrhages.

The tangible clinical symptoms are intestinal hæmorrhage of unexplained origin and abdominal pain of vague and indefinite character. The pathological findings are the presence in the diverticulum of aberrant gastric mucosa, and ulceration located in the area where gastric and intestinal mucosa merge. The course of the disease tends to ulceration of the mucosa, erosion of blood-vessels, penetration of the diverticular wall, and perforation into the peritoneal cavity.

Peptic ulcer may occur without intestinal hæmorrhage, but as this paper deals more particularly with the symptomatic value of intestinal hæmorrhage associated with peptic ulcer, I shall not go into the question of peptic ulcer unassociated with hæmorrhage. In such instances there are no pre-perforative symptoms which will lead to a correct diagnosis, and neither has X-ray nor any other laboratory agency proven of value in revealing the presence of a Meckel's diverticulum. These cases come to operation when signs of acute abdominal disease demand exploration, and a perforation of the diverticulum is usually found.

Meckel's diverticulum is present in approximately 2.5 per cent. of humans, and largely predominates in males.

There are three main types, and Christie,² from a study of sixty-three autopsy specimens from the laboratory of the Baby's Hospital, N. Y., gives the following percentages: Type 1—The umbilical fistula, 6.3 per cent. Type 2—Partial obliteration with fibrous band running from the tip of the diverticulum to the umbilicus or some adjacent structure, 10 per cent. Type 3—The typical diverticulum given off from the antimesenteric side of the ileum, lying free in the peritoneal cavity, and presenting a closed distal extremity, 82.5 per cent.

Less frequently observed are: Type 4—The giant diverticulum of bizarre form or shape, sometimes coming off from the mesenteric side of the ileum and developing between the folds of the mesentery. Type 5—The umbilical polyp, either attached to the remains of the omphalomesenteric duct inside the abdomen, or entirely cut off from internal connections.

In Types 1 and 5 the diagnosis is made by inspection and the indications for treatment are obvious. From Type 2 we obtain the greatest number of cases of obstruction. Type 3 gives rise to intussusception, volvulus and diverticulitis, and is the one in which peptic ulcer has been most frequently observed. Type 4 gives rise to problems peculiar to the individual case.

As recently as 1913, peptic ulcer of Meckel's diverticulum was not generally recognized; and neither Meyer,³ in 1912, nor Wellington,⁴ in 1913, mention the condition, though both carefully reviewed diseases of the diverticulum. Likewise, until very recently, so little attention had been given to the histology that the significance of aberrant gastric mucosa was not appreciated in the few instances in which it had been observed. Kelly and Hurdon,⁵ in 1905, Adami and Nicholls,⁶ in 1911, and Cullen,⁷ in 1916, say, "the walls and mucosa are similar to those of the intestine"; Adami and Nicholls adding that "the diverticulum may become strangulated or inflamed, or that it may perforate." Investigations of Schaetz,⁸ in 1925, changed our conception of the structure of these diverticula. He studied in serial section thirty diverticula, and found that in only seventeen, or 57 per cent., was the mucosa similar to that of the adjacent ileum. His further findings were as follows: Five, or 16.6 per cent., showed islands of gastric mucosa. One showed pancreatic tissue. Two showed both pancreatic tissue and gastric mucosa. One showed carcinoid mucosa. One showed mucosa of doubtful heteroplasia. As usually quoted, it is said that his statistics showed gastric mucosa in 16.6 per cent., whereas he found it in 23.3 per cent., the additional cases showing both gastric mucosa and pancreatic tissue.

Deetz states that Zenker found aberrant pancreatic tissue in a Meckel's diverticulum as far back as 1861, and this observation has been confirmed many times since. Its presence, so far, has given rise to no clinical manifestations. Bookman⁹ recently reported a carcinoma of the duodenum originating in an area of aberrant pancreatic tissue, and this gives rise to interesting speculation in regard to such possibility in a Meckel's diverticulum.

The earliest observation of aberrant gastric mucosa in the remains of the omphalomesenteric duct was that of Tillmanns,¹⁰ in 1881.⁷ He found this not a Meckel's diverticulum proper, but in an umbilical polyp. The case was reported as one of "Congenital prolapse of gastric mucosa through the umbilical ring." This explanation was accepted for a time, but further study of a series of similar cases proved that the gastric mucosa was in the remains of the omphalomesenteric duct, and that it did not result from herniation of gastric mucosa.

Cullen has summed up the evidence presented by the reported cases of umbilical polyps and is of the opinion that they are remnants of the omphalomesenteric duct.

HÆMORRHAGE FROM MECKEL'S DIVERTICULUM

Earliest Cases.—In 1903, Hilgenreiner¹² reported the case of a boy of eighteen years, who, since childhood, had had bloody stools at various times, and many attacks of severe abdominal pain. A tender mass appeared at the right of the umbilicus and a diagnosis of appendicitis was made.

At operation there was found a Meckel's diverticulum seven centimetres long attached by its distal extremity to the abdominal wall. It was resected, and was found to contain an ulcer which had penetrated deeply into the wall of the diverticulum. While it was not recognized as such, Stulz and Woringer,¹³ in reviewing the case, say that the histological report, and especially the wood cut which illustrated the paper, shows that the case is one of chronic peptic ulcer.

In 1907, Deetz¹ made the first suggestion concerning the peptic nature of an ulcer in Meckel's diverticulum. A boy nine years of age became suddenly ill with symptoms of diffuse peritonitis, which was diagnosed as being due to perforation of the appendix. At operation the peritonitis was found to be due to perforation at the base of a Meckel's diverticulum. Histological examination showed the presence of gastric mucosa. There had been no intestinal bleeding.

His study of the case convinced him of the peptic nature of the ulceration, and in further comment he says: "It will be necessary in the future to search for gastric mucosa in extirpated diverticula," for "I imagine that in this form of diverticulitis when it comes to ulceration, conditions may be at work which are similar to those which are present in true gastric ulcer."

He says that he has found reference to only one similar case in the literature, that of Hildebrandt,¹⁵ recorded in *Charity Annalen*, 1905, and that Hildebrandt referred only casually to the finding of the aberrant gastric mucosa.

In 1911, Callender¹⁶ in an autopsy on an infant who died of intestinal hæmorrhage, made the first observation of a bleeding ulcer of Meckel's diverticulum in which the presence of gastric mucosa was definitely confirmed by histological examination. His case was not reported, however, until 1915.

In 1913, Hubschmann¹⁷ reported the case of a boy who, following a fall on the abdomen, had intestinal bleeding for four weeks, followed by symptoms of peritonitis. At operation diffuse suppurative peritonitis was found, but the source of the infection was not discovered until autopsy. A perforated ulcer of Meckel's diverticulum was found with erosion of a blood-vessel. He made an exhaustive study of the pathological features of this ulcer, and classed it as a definite peptic ulcer, and demonstrated in the sections the presence of gastric mucosa.

In 1914, Griffith¹⁴ published the first detailed report in American literature of ulceration of Meckel's diverticulum where intestinal hæmorrhage was a marked symptom and where autopsy confirmed the source of the bleeding. He mentions Hubschmann's case of peptic ulcer, but lays no stress on peptic ulcer as a probable factor in his own case, and submits no histological studies.

These early cases may be considered somewhat fundamental in establishing intestinal hæmorrhage as a symptom of ulceration of Meckel's diverticulum and the presence of gastric mucosa as a cause of the ulceration. The cases in this report give ample confirmation to these claims.

In stressing the diagnostic importance of intestinal hæmorrhage, we must review the relation of hæmorrhage and pain to time of operation or autopsy. In one instance (Abstract No. 5) pain of fourteen days' duration was followed by intestinal hæmorrhage and signs of suddenly developing peritonitis. A perforation was found. In one instance (Abstract No. 18) recurring hæmorrhages had been noted for twelve years. An inflamed diverticulum, supplied with large vessels, was found, but the presence of an ulcer was not

demonstrated. In nine cases with acute onset, hæmorrhage and pain appeared at practically the same time (Abstracts Nos. 4, 14, 16, 21, 22, 24, 25, 31 and 33). Four of these showed perforated ulcers (Abstracts Nos. 14, 16, 22 and 31), and five showed ulcers in various pre-perforative stages. In the remaining twenty-two, autopsy or operation was preceded by hæmorrhage for periods varying from a few days to many months, or even years. In these twenty-two cases were found twelve perforated ulcers. In every instance operation could have been carried out at a pre-perforative stage, with a vastly lowered mortality, if the diagnostic significance of intestinal hæmorrhage had been fully appreciated.

Two cases present features of unusual interest and are reported in brief to emphasize the importance of intestinal bleeding as an indication of ulceration of the diverticulum; also, as pointing to the necessity of removing wherever possible all diverticula found in the course of abdominal operations.

The case of Brasser, 1924 (Abstract No. 8). Pain in lower abdomen; ten days later repeated hæmorrhages; operation revealed colon filled with blood but the source was not ascertained and the abdomen was closed: Death from peritonitis eight days later. Autopsy. Perforation of Meckel's diverticulum.

The case of Winkelbauer, 1929 (Abstract No. 24). Abdominal pain followed by bloody stool. Diagnosis, intussusception; operation; diverticulum with band incarcerating ileum; band divided and incarceration relieved. Intestinal bleeding continued, and two months later the abdomen was reopened, when an intussusception of the diverticulum into the ileum was found. The diverticulum showed a peptic ulcer which had eroded a vessel.

The case of Pascale (Abstract No. 15) is also of special interest on account of the findings. In a woman of forty-one years with history of digestive disturbance since seventeen years of age, and of intestinal hæmorrhage since the age of twenty-nine, a completely healed peptic ulcer of Meckel's diverticulum was found; the only one so far observed.

Histology.—Histological studies are reported in twenty-five instances. In twenty-three of these gastric mucosa was found.

In the case of Hilgenreiner (Abstract No. 1) the first bleeding diverticular ulcer recorded, nothing is said concerning the peptic nature of the ulcer, and the histological examination showed "normal structure of ileum, small intestine structure with hyperplasia of glands, lower villi, and more numerous goblet cells." Stulz and Woringer have reviewed this case and claim that the histological examination and particularly the cut which illustrates the paper prove the case to be one of chronic peptic ulcer.

In Winkelbauer's case (Abstract No. 25) the histological report states that, "The preparation showed a peptic ulcer with erosion of a branch of an artery." In the section examined, neither gastric mucosa nor pancreas tissue could be determined.

In eight instances no histological examinations were made. This omission was due in one instance to the necrotic state of the diverticulum making section impossible (Abstract No. 17); in another instance to the method of treatment, exteriorization of the diverticulum allowing it to be cast off after becoming necrotic (Abstract No. 16); in another, to the loss of the specimen in the laboratory (Abstract No. 11).

Operative and Autopsy Findings.—In the thirty-three cases analyzed, perforation was found in sixteen instances and in sixteen instances nonperforating ulcers were found. In one case an inflamed diverticulum was found but ulcer was not demonstrated.

Three perforating and two nonperforating ulcers were treated medically. All died; one, however, died from intercurrent disease.

HÆMORRHAGE FROM MECKEL'S DIVERTICULUM

TABLE I

Mortality

Total Cases	Recovered	Died	Mortality
33	22	11	33.33
Treated medically			
5	0	5	100.
Perforating ulcers treated surgically			
14	8	6	42.86
Nonperforating ulcers treated surgically			
13	13	0	00.
Inflamed diverticulum treated surgically			
1	1	0	00.

TABLE II

Peptic Ulcer of Meckel's Diverticulum, a Disease of Infancy and Childhood Appearing Principally in Males

Age and Sex in This Series

Males	28.	Females	3.	Sex Not Stated	2.
Ages					
In the first year					6
In the second year					8
From 3 to 5					4
5 to 10					4
10 to 15					8
Over 15					3
Total					33

The age of the youngest was fifteen weeks and of the oldest forty-one years.

In those patients over fifteen years, the ages were eighteen, twenty-eight, and forty-one, respectively.

In the first two the history of intestinal bleeding went back to early childhood. In the patient of forty-one years of age, digestive disturbances had been noted since the age of seventeen, and bleeding since the age of twenty-nine.

TABLE III

Pre-operative Diagnoses

Appendicitis	2
Intestinal obstruction or intussusception	7
Ulceration of intestinal tract	4
Ileocecal tuberculosis	2
Intestinal polyp or tumor	1
Exploration to ascertain source of hæmorrhage or peritonitis	13
Bleeding from ulceration of Meckel's diverticulum	4
Total	33

The four cases correctly diagnosed before operation were reported since 1927.

These correct diagnoses were evidently due to a wider recognition of intestinal bleeding as symptomatic of ulcer of Meckel's diverticulum.

Greenwald and Steiner (Abstract No. 32) made their diagnoses on the history of bleeding and pain, and confirmed the diagnosis of perforation by fluoroscopy, when they found a column of air between the liver and the diaphragm.

MASON AND GRAHAM

TABLE IV

Treatment Consists in Removing the Diverticulum in the Manner Best Suited to the Individual Case

In This Series the Following Methods Were Employed
with the Results Noted

	No.	Rec.	Died
Drainage: perforation found at autopsy.....	2		2
Exploration: abdomen closed. Perforation found at autopsy.....	1		1
Drainage: Secondary removal of diverticulum.....	1	1	
Suture of ulcer: secondary removal of diverticulum.....	1	1	
Diverticulum fixed in wound and allowed to slough.....	1		1
Resection of intestine with diverticulum.....	4	4	
Resection of diverticulum.....	18	16	2
Treated medically.....	5		5
Total.....	33	22	11

CASE REPORT.—*Intestinal Hemorrhage from Peptic Ulcer of Meckel's Diverticulum.*—Stanley W., white male, aged nine months, was sent to the Children's Hospital, of Birmingham, Ala., September 24, 1929, by Dr. S. P. Wainwright, who had seen him at home a few hours earlier. The child had enjoyed good health until one week before admission, when bowels became loose and watery. On the afternoon of September 24, he had a rather large bloody stool, and was taken to the hospital. He had a normal stool on the morning of the twenty-fifth, after which bleeding recurred. On examination about 10:30 A.M., by Dr. Russell Callen, the Attending Pædiatrician, it was noted that the child was passing dark fluid blood unmixed with fæces. There were no other symptoms. The child was in good humor and showed no evidence of pain. He did not appear to be ill, except for marked pallor. The hæmoglobin was 46 per cent.; red blood count showed 2,200,000 cells; the total white count, 5,650; and the differential count showed small lymphocytes, 29 per cent.; large mononuclear lymphocytes, 10 per cent.; polymorphonuclear leucocytes, 61 per cent.

Physical examination by members of the pædiatric staff failed to reveal any cause for the hæmorrhage. A barium enema not only failed to reveal any diagnostic assistance, but proved actually misleading, in that the enema advanced only to the hepatic flexure, giving rise to the suspicion of a possible incomplete intussusception. Evidently an insufficient amount of fluid was employed or sufficient time had not elapsed for the enema to advance farther; for neither the history, the examination of the abdomen, nor the appearance of the patient bore out the diagnosis of intussusception; and examination of the hepatic flexure at operation showed no obstruction or other abnormality.

Exploration was carried out under ether at 5:30 P.M. The hepatic flexure was first examined for the reason above set forth. The appendix, quite normal in appearance, was removed. Further search revealed a Meckel's diverticulum thirty-five centimetres above the ileocecal valve. The lumen was almost that of the adjacent ileum; the length was approximately six centimetres; the tip was free and rather nodular. The diverticulum was removed as the possible source of the hæmorrhage. It was cut off flush with the ileum and the opening was closed with two rows of Lembert sutures. There was no blood in the diverticulum at the time of its removal. The patient made a prompt recovery.

Microscopical Description by Dr. George S. Graham.—The specimen was fixed without opening and sections were made longitudinally throughout its whole length. They show a pouch of intestine with normal muscular and serous layers in the wall. The base where the diverticulum was amputated from the intestine is lined by mucous

HÆMORRHAGE FROM MECKEL'S DIVERTICULUM

membrane of small intestine type. This is abruptly replaced at a short distance from amputated end by gastric mucosa with characteristic glands containing chief and parietal cells and gastric pits lined by mucus-secreting cells. This lines the whole remaining portion of the lumen on both walls and at the blind end. The submucosa and mucosa are elevated into several high folds. At tip of the diverticulum there is a relatively large mass of glandular tissue of pancreatic type. It lies for the most part outside the muscular coat of the diverticulum but a small lobule penetrates the submucosa. The duct system is well developed. On one lateral wall at the place where the two mucosal types meet the gastric mucosa is destroyed by ulceration. The destruction extends over a sector nearly one-fourth of the length of the lateral wall on which it is located. At the base of a submucosal fold it terminates in a deeper area of destruction within whose floor there is a small arteriole stuffed with red cells and partially surrounded by the necrotic tissue of the floor. Just beneath it are two other cross-sections of small arteriole, probably the same vessel. The intestinal wall beneath the ulcer is infiltrated



FIG. 1.—Mass of pancreatic gland tissue lying upon muscular wall at tip of diverticulum. ($\times 12$.)

to the peritoneal surface by large numbers of lymphocytes among which there is a considerable percentage of neutrophils and eosinophiles. (Figs. 1, 2, and 3.)

Microscopical Diagnosis.—Chronic peptic ulcer in Meckel's diverticulum.

Cases of Meckel's Diverticula of Unusual Form, Size, and Development Which Have Been Associated with Intestinal Hæmorrhage Have Been Reported by Moll,⁴² Tisdall,⁴³ and Abt and Strauss.⁴⁴—The bleeding in these cases has probably come about by interference with the circulation of the intestine resulting from the unusual anatomical peculiarities rather than from ulceration. In Moll's patient the diverticulum was thirty-three inches long, and all layers of the small intestine were present. Two ulcers were found at the junction with the small intestine. In the patient of Tisdall's, a Meckel's diverticulum fifty-nine centimetres long was attached to the ileum forty-five centimetres above the ileocecal valve. The distal extremity was expanded into a pouch as large as the stomach. Many gastric cells were present but there was no ulceration. In the case of Abt and Strauss the diverticulum was eighteen inches in length and had developed between the leaves of the mesentery. There was no ulceration and the sections showed only intestinal mucosa.

The Question of Ulceration and Hæmorrhage Without the Presence of Aberrant Gastric Mucosa.—The cases of Hilgenreiner and Winkelbauer raise the question of bleeding from ulcers other than those showing aberrant gastric mucosa.

Hilgenreiner did not mention the finding of gastric mucosa in his case, but, as already noted, Stulz and Woringer claim that the case is one of proven chronic peptic ulcer.

Winkelbauer diagnosed his case as one of peptic ulcer, but says that "in the sections examined neither gastric mucosa nor pancreas tissue could be determined." One's only comment on this is that further search might possibly have revealed the presence of gastric mucosa.

The Claim is Made That Diverticulitis is Distinctly Different from Peptic Ulcer.—The latter has a definite location in that area of the diverticulum or in the adjacent ileum where gastric mucosa merges with that of the ileum.

This ulcer, as Stulz and Woringer¹¹ hold, is "mostly of acute evolution, opening vessels, penetrating into neighboring organs and making its way toward the free peritoneum; it then perforates and provokes diffuse or limited peritonitis."



FIG. 2.

FIG. 2.—Mucosal ulcer. The ulcer begins abruptly at base of a ruga-like fold and extends almost to amputation level. ($\times 12$.)

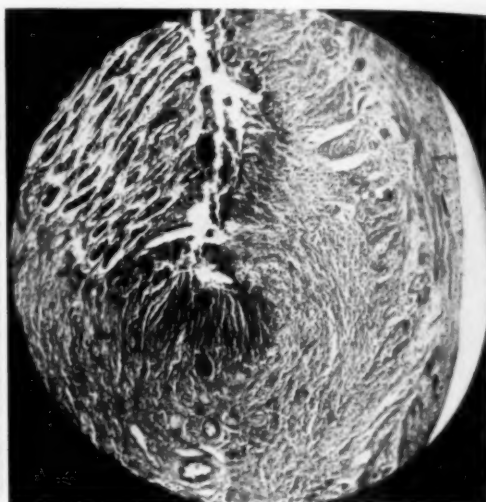


FIG. 3.

FIG. 3.—Higher power view of ulcer margin. At base of zone of necrosis can be seen an engorged arteriole. ($\times 48$.)

We do not know the causes that lead to ulceration about these little areas of misplaced gastric mucosa, but the evidence is strong that the influence of the acid secretion from the gastric cells, as it comes in contact with the alkaline secretion from the intestine, causes a break in the mucosa and produces an ulcer which Hübschmann likens to the gastrojejunal ulcer following gastroenterostomy. These are questions for academic discussion by pathologists. The important surgical considerations are:

First.—To recognize that intestinal hæmorrhage of unexplained origin, especially occurring in a child, may be due to peptic ulcer of Meckel's diverticulum; that the tendency of the peptic ulcer is to perforate; and that operation should be undertaken before perforation has taken place.

Second.—In exploring for the purpose of locating the source of intestinal hæmorrhage or diffuse peritonitis, to remember that they are often to be found in Meckel's diverticulum.

HÆMORRHAGE FROM MECKEL'S DIVERTICULUM

Third.—To remove, whenever possible, any Meckel's diverticulum found at operation as a measure to prevent possible future trouble.

ABSTRACT OF CASES ANALYZED FROM LITERATURE

No. 1.—Hilgenreiner,¹⁸ 1903. Male, aged eighteen years. For several years violent attacks of abdominal pain with constipation and bloody stools. On one occasion there was a large intestinal hæmorrhage. A tender mass developed on the right side of the umbilicus, and a diagnosis of appendicitis was made. The mass was three by six centimetres in size. *Operation.*—The tumor proved to be a Meckel's diverticulum seven centimetres long attached by its distal extremity to the abdominal wall. The diverticulum together with the tumefied and inflamed area of abdominal wall was resected, with recovery.

On section there was found an ulcer which had deeply penetrated the wall of the diverticulum. *Histological Examination.*—In the central portion, normal structure of the ileum; in the peripheral, small intestine structure with hyperplasia of glands, lower villi, and more numerous goblet cells.

No. 2.—Hubschmann,¹² 1913. Male, aged four and one-half years. Abdominal trauma was followed by intestinal hæmorrhage for four weeks, when signs of diffuse peritonitis appeared. Operation revealed free pus in the peritoneal cavity but the source of the infection was not ascertained. At autopsy a Meckel's diverticulum four centimetres long was found. The tip was free and a perforating ulcer was found at the base. This had eroded a blood-vessel.

No. 3.—Griffith,¹⁴ 1914. Male, aged nineteen months. Infant under observation for three months for abdominal pain and intestinal bleeding. No diagnosis other than ulceration of intestinal tract. Death. *Autopsy.*—Meckel's diverticulum three centimetres long, lying in centre of an abscess. Mucosa showed an ulcer at tip, and purulent exudate on serous surface corresponded to location of ulcer. Tip was free. No histological studies.

No. 4.—Callender,¹⁵ 1915. Infant, nineteen months of age; death after thirty-six hours from intestinal hæmorrhage. *Autopsy report.*—Diverticulum two centimetres long attached by tip to posterior wall of cæcum. Punched-out ulcer 0.5 centimetre in diameter in ileum at border of diverticulum. At margin a small vessel is found plugged with clot. Mucosa shows gastric fundus glands.

No. 5.—Muller,¹⁷ 1919. Male, aged eleven years. For past fourteen days pain in right lower abdomen and slight diarrhoea. The following night he had severe pain and passed a very black stool. He was admitted at the hospital at 10 P.M. with a diagnosis of appendicidal peritonitis. *Operation.*—Thirty-seven centimetres above the ileocecal valve was found a Meckel's diverticulum seven centimetres long with a perforation near the attachment to the ileum. The perforation was closed by suture and the abdomen was drained. Two months later a secondary operation was undertaken for the removal of the diverticulum. A segment of small intestine together with the diverticulum was resected, with recovery. Histological sections showed that the mucosa throughout its greater portion was similar to that of the fundus of the stomach.

No. 6.—Meulengracht,¹⁸ 1919. Male, aged twelve years. Ten days before admission to the hospital acute suppurative otitis media developed in connection with septic endocarditis. He had several attacks of indefinite abdominal pain with vomiting, and severe melæna appeared fourteen days before death and persisted for several days. *Autopsy.*—One hundred and twenty centimetres above ileocecal valve was found a Meckel's diverticulum. On the floor of the diverticulum was an ulcer one by one and one-half centimetres. The ulcer lay in the portion of the diverticulum lined with intestinal mucosa, adjacent to an area of gastric mucosa.

No. 7.—Megevaud and Dunant,¹⁹ 1922. Male, aged twenty-eight years, intestinal hæmorrhages since early childhood, with many attacks of abdominal pain. On June 21

and 22, 1918, a large amount of blood was passed by bowels. At 9:30 P.M. the patient was almost in collapse. There was no definite diagnosis but duodenal ulcer was considered probable. *Operation*.—No ulcer of the stomach or duodenum was found. There was no blood in the small intestines but a large amount was found in the colon. A Meckel's diverticulum five and one-half centimetres long was found about forty centimetres above the ileocecal valve. The diverticulum was excised, with recovery. The diverticulum was lined for the most part with gastric mucosa; at junction of gastric with intestinal mucosa was a peptic ulcer with erosion of vessels.

No. 8.—Brasser,²⁰ 1924. Male, aged fifteen years. Pain in lower abdomen; ten days later repeated intestinal hæmorrhages. *Diagnosis*.—Intestinal polyp tumor or tumor of colon. *Operation*.—Colon filled with blood but source not found. Abdomen closed. Eight days later sudden development of peritonitis, with death. *Autopsy*.—Meckel's diverticulum with clubbed and attached to appendix. Perforation at base, with ulcer located at line of transition of gastric in intestinal mucosa.

No. 9.—Guibal,²¹ 1924. Male, aged fourteen years. Painless intestinal hæmorrhage recurring over a period of six months; later symptoms of right renal colic. *Diagnosis* not definite, but ileocecal tuberculosis suspected. *Operation*.—A Meckel's diverticulum seven centimetres long, with clubbed end; perforation two centimetres above its opening into the intestine, at a point of junction of intestinal and gastric mucosa. Resection of twenty centimetres of ileum, with recovery.

No. 10.—Humbert,²² 1924. Male, aged eleven months. Intestinal hæmorrhages at five and eight months. Present attack sudden onset with abdominal pain and other evidence of acute intra-abdominal disease. Became progressively worse. *Diagnosis*.—Perforative peritonitis, probably not of appendiceal origin, as most of the symptoms were in the median line and to the left. *Operation*.—Abdomen opened, with immediate escape of gas and pus. Bladder accidentally incised and sutured. Drainage was instituted and the wound closed. Death. Autopsy revealed a Meckel's diverticulum one by three centimetres with conical, free, distal end. There was a perforated ulcer at the exact junction of intestinal with gastric mucosa.

No. 11.—Jackson, R. H.,²³ 1924. Male, aged ten years. Recurring hæmorrhages and left-sided abdominal pain for four years. No diagnosis was arrived at, and operation was undertaken for the purpose of exploring for the source of the hæmorrhage. An indurated Meckel's diverticulum was found three by six centimetres, coming off from the ileum fifty centimetres above the ileocecal valve. Twelve centimetres of ileum, with the diverticulum, were resected, with recovery. An indurated ulcer was found at the junction of the ileum with the diverticulum, about four-fifths of the ulcer lying in the diverticulum. The specimen was lost in transit to the laboratory, hence no histological sections were made.

No. 12.—Abt and Strauss,²⁴ 1925. Female, aged two years. Recurring hæmorrhages and slight abdominal pain for four months. Operation revealed a large inflammatory mass imbedded in the mesentery. Mass resected, with part of ileum; end-to-end anastomosis. In the mass was found an ulcerated Meckel's diverticulum, with remnants of gastric mucosa at apex, with recovery.

No. 13.—Abt and Strauss. Male, aged eleven months. Intestinal hæmorrhages for two months, with severe pain for a short time before operation. Exploration on account of bleeding. No diagnosis made. Meckel's diverticulum found two and one-half inches above ileocecal valve. Distal end infiltrated and attached to cæcum and appendix. It was filled with blood and there were several ulcers at the tip. Histology not reported.

No. 14.—Ulrich,²⁵ 1925. Male, aged eight years. On the morning of admission had three bloody stools but no pain. During the next three days, one or two bloody stools each day. On the fourth day became acutely ill, with fever, pain, constipation, and abdominal rigidity. No definite diagnosis. *Operation*.—Perforated Meckel's diverticulum two and one-half centimetres long, adherent to right side of pelvis by a strand which emanated from the tip. Excision of diverticulum, with death. *Histological*

HÆMORRHAGE FROM MECKEL'S DIVERTICULUM

Examination.—Lower portion of the diverticulum was lined with intestinal mucosa, above this was typical gastric mucosa.

No. 15.—Pascale,²⁴ 1925. Woman, aged forty-one years. Since seventeen years of age had suffered from abdominal pains and indigestion. After about eleven years the pain became definite in the para-umbilical region on the right side. One year later following a severe attack of pain there was a bloody stool. Other similar attacks occurred at long intervals. Up to this time the diagnosis had been recurring appendicitis. Pascale ruled this out, and made a diagnosis of ulcer of the small intestine. *Operation.*—There was found a Meckel's diverticulum two centimetres long, with free distal end, which was removed, with recovery. *Histological Examination.*—On opening the diverticulum a fecal concretion was found; also a cicatrized ulcer. Gastric mucosa was present. The findings indicated that there had been a round ulcer of the diverticulum which had healed spontaneously.

No. 16.—Stulz and Woringer,²¹ 1926. Male, aged four years. Sudden onset with abdominal pain, vomiting, and intestinal hæmorrhage. Was seen on eighth day. *Probable Diagnosis.*—Intussusception. *Operation.*—Meckel's diverticulum size of an adult thumb, with perforation at base. Mesenteric vessels leading to diverticulum were ligated; the diverticulum was fixed to the parietal peritoneum and allowed to become gangrenous, when it was snipped off. No sections of the diverticulum were possible. Death from secondary peritonitis.

No. 17.—Stulz and Woringer. Male, aged eleven months. Was under observation twelve days when child died. *Autopsy.*—Meckel's diverticulum size of a child's thumb fixed to peritoneum in right paravesical region by a fibrous band. There was a small peridiverticular abscess, and a perforated ulcer with clean-cut border at the margin of the intestinal and diverticular mucosa. No histological sections could be made.

No. 18.—Mayo and Johnson,²⁵ 1926. Male, aged fifteen years. Appendicitis, followed by two intestinal hæmorrhages occurred when three years of age. At age of twelve had two attacks of appendicitis within three months. The ruptured appendix was removed. Three weeks later had intestinal hæmorrhage. Repeated hæmorrhages with epigastric pain continued at intervals for the next three years. Abdominal exploration, no pre-operative diagnosis. Exploration of stomach, duodenum, pancreas, gall-bladder, liver and colon was negative. Beginning at the duodenojejunal angle, the small intestine was examined inch by inch, to a site forty-five centimetres above the ileocecal valve, where an inflamed, oedematous Meckel's diverticulum was found. It was profusely supplied with large blood-vessels; it was resected. The patient recovered. No pathological report is submitted. The presence of ulcer is not mentioned.

No. 19.—Kleinschmidt,²⁵ 1927. Male, aged fifteen years; for one and one-half years pain in right lower abdomen. Nine months before admission, severe intestinal hæmorrhage with pain and vomiting. On admission diagnosis of gastric ulcer was made and he was placed on ulcer treatment for nineteen days, when sudden violent pain in the right lower abdomen suggested acute appendicitis. *Operation.*—There was found a Meckel's diverticulum three by six centimetres attached to the umbilicus. The diverticulum perforated near its attachment to the ileum. The diverticulum was resected, with recovery. The diverticulum was entirely lined with gastric mucosa.

No. 20.—McCalla,²⁶ 1927. Male, aged three years and ten months. Recurring hæmorrhages since eleven months of age with some abdominal pain. For four months has been well except for slight abdominal pain. On August 14 felt unusually well, but during the night had severe abdominal pain, sank rapidly and died. Autopsy revealed a Meckel's diverticulum with perforation at the base. The ulcer was located at a point where the intestinal and gastric mucosa merged.

No. 21.—Jackson, A. S.,²⁴ 1927. Male, aged fourteen years. Severe generalized abdominal pain followed three days later by intestinal hæmorrhage. He was seen on the fourth day by Dr. E. A. Ketterer, the same physician who had about ten years before sent a patient with intestinal hæmorrhage to Dr. R. H. Jackson, which proved

to be due to a bleeding ulcer of Meckel's diverticulum. This physician, from his observation of the case of R. H. Jackson, made a diagnosis in this case of bleeding of Meckel's diverticulum. Further hæmorrhages continued until the patient was exsanguinated, and required several transfusions before operation. Operation revealed a Meckel's diverticulum three by eight centimetres; distal end was free, and presented a puckered appearance. The diverticulum was excised, with recovery. Pathological examination revealed an ulcer and the diverticulum showed areas of gastric mucosa.

No. 22.—Meiss,²⁷ 1928. Child, aged two years. Sudden severe abdominal pain of few minutes' duration but recurring frequently. Twenty-four hours before admission had very large bloody stool with little or no pain. No diagnosis was made further than intestinal hæmorrhage of undetermined origin. *Operation*.—There was a Meckel's diverticulum three centimetres long with tip infiltrated and adherent to ileum, into which it had perforated. The diverticulum was excised, with recovery. *Histological Examination*.—Intestinal mucosa was found in the portion of the diverticulum near the ileum, with sudden transition to gastric mucosa, which lined the greater part of the diverticulum.

No. 23.—Peterman and Seegar,³⁰ 1928. Male, aged six years. Boy was struck in groin by wagon tongue. There was pain and vomiting for two days, also marked anaemia. *Diagnosis*.—Acute appendicitis. *Operation*.—Much blood in abdominal cavity. Drainage instituted and wound closed. Some time later there were repeated hæmorrhages from the bowel associated with pain and tenderness about the umbilicus. *Diagnosis*.—Bleeding from Meckel's diverticulum. *Operation*.—A Meckel's diverticulum was found forty-five centimetres from the ileocecal valve. It was four centimetres long, with the tip attached to the ileum eleven and one-half centimetres above the point of origin of the diverticulum. An ulcer had perforated from the tip into the ileum. Twenty-eight centimetres of ileum with the diverticulum were resected, with recovery. The tip was lined with gastric mucosa. Two ulcers were also found in the ileum and one in the base of the diverticulum.

No. 24.—Winkelbauer,²⁸ 1929. Male, aged two years. Abdominal pain followed in a short time by 200 cubic centimetres of bright red blood. Abdomen soft and only slightly tender to pressure on right side. Probable diagnosis; intussusception. *Operation*.—No intussusception found. There was found a Meckel's diverticulum three centimetres long with œdematous walls. At one spot was a more notable hardening, and a bleeding ulcer was suspected. The diverticulum was excised. Recovery. On opening the diverticulum was a shallow ulcer in the border of the ileum separated by a narrow zone from an island of gastric mucosa.

No. 25.—Winkelbauer. Male, aged nineteen months. A few hours before coming to a physician had been taken ill with abdominal pain and vomiting, and a passage by bowels of about one-eighth of a litre of blood. The abdomen was soft and not tender. He had a second intestinal hæmorrhage. Intussusception was suspected. *Operation*.—There was found a Meckel's diverticulum from the apex of which a strand extended toward the small intestine where it was fixed. A loop of small intestine was incarcerated by the strand. The colon was filled with blood but the cause of the hæmorrhage was not determined; the incarcerated intestine was freed and the abdomen was closed. Two months later the patient returned because of recurrence of intestinal hæmorrhages. *Operation*.—In the middle of the ileum there was an invagination of the diverticulum fixed by adhesions. It contained an ulcer. The diverticulum was extirpated, with recovery. *Histological Examination*.—The preparation showed a peptic ulcer with erosion of a branch of an artery. In the sections examined neither gastric mucosa nor pancreas tissue could be determined.

No. 26.—Schwarz and Daly,³⁰ 1929. Male, aged eight years. Patient suffered from intestinal hæmorrhages, abdominal pain and cramps, for several days. Severe anaemia was noted. He was kept under observation for three days, and a diagnosis of bleeding from ulcer of Meckel's diverticulum was made. Operation revealed an elongated

HÆMORRHAGE FROM MECKEL'S DIVERTICULUM

Meckel's diverticulum, which was removed. Recovery. The diverticulum contained an ulcer which had eroded a large artery. No histological studies are presented.

No. 27.—Smith and Hill,²⁷ 1928. Male, aged fourteen months. Intestinal hæmorrhage was followed four days later by vomiting, abdominal pain, visible peristalsis, and abdominal distension, and a mass was detected in right lower abdomen. *Diagnosis*.—Intestinal obstruction of uncertain origin. *Operation*.—Meckel's diverticulum four centimetres in length, perforated and gangrenous at distal end. Secondary obstruction from adhesions. Resected. Recovery. No pathological report.

No. 28.—Aschner and Karelitz,²⁸ 1930. Female, aged fifteen months. Pallor, vomiting, fever, for five days; followed by blood in stool and a tender mass in right lower abdomen. Was sent to hospital with diagnosis of Meckel's diverticulum. At hospital it was thought that the condition was intussusception. *Operation*.—No intussusception. An inflamed diverticulum four centimetres long was found, attached by a fibrous strand to the umbilicus. A loop of intestine passed under this and several loops were matted together by adhesions. The diverticulum was freed from the umbilicus and the adherent intestines were freed. The wound was closed. *Secondary Operation*.—Sixteen days later for removal of the diverticulum. The diverticulum was lined throughout with gastric mucosa, and there was a chronic penetrating ulcer situated in mucosa, of intestinal type, but immediately adjoining mucosa of gastric type.

No. 29.—Aschner and Karelitz. Male, aged twenty-six months. Repeated attacks of intestinal hæmorrhage for nine months. The later attacks were associated with pain. *Diagnosis*.—Recurring intussusception. *Operation*.—(Dr. A. V. Moschowitz.) A Meckel's diverticulum inflamed and indurated, was found eighteen inches above ileocecal valve. It was excised and patient recovered. Histological examination showed an ulcer at the neck of the diverticulum at the junction of intestinal and gastric types of mucosa.

No. 30.—Fevre, Patel and Lapart,²⁹ 1930. Male, aged five months. The day before he was seen by a physician had several black stools but was not otherwise ill. On the following morning he was seized with sudden violent abdominal pain and vomiting, accompanied by fever and another bloody stool. *Diagnosis*.—Intussusception. *Operation*.—No intussusception found. There was a short thick Meckel's diverticulum three centimetres long adherent to the ileum with a perforated ulcer at the base. Diverticulum removed, with recovery. *Histological Examination*.—The perforation was located in an ulcer on the intestinal mucosa immediately below an area of gastric mucosa.

No. 31.—von Haberer,³⁰ 1930. Male, aged thirteen years, appendectomy for colicky pains about umbilicus. Relief for four weeks then return of pain for two months; further periods of relief, then return of pain. For seven weeks previous to admission had several tarry stools, and became very anæmic. Ileocecal tuberculosis was suspected. *Operation*.—Massive adhesions about descending colon and bladder, and in the mass was a hard tumor, on freeing which a long perforated Meckel's diverticulum was found. The diverticulum, together with the cæcum and 1.3 centimetres of ileum resected, with recovery. *Histological Report*.—Base of the diverticulum was lined with small intestinal mucosa, upper part showed gastric mucosa. The perforated ulcer was located at the boundary between the gastric and intestinal mucosa.

No. 32.—Greenwald and Steiner,³¹ 1931. Male, aged fifteen weeks. Patient had two large tarry stools associated with pain and restlessness. Two weeks later had sudden attack of abdominal pain, vomiting and fever. Fluoroscopical examination revealed a column of air between liver and diaphragm. *Diagnosis*.—Perforated Meckel's diverticulum. *Operation*.—Meckel's diverticulum size of hazelnut was found, with perforation near base. The diverticulum was excised, with death resulting. The diverticulum showed a punched-out perforated ulcer near the base. The mucosa showed areas of gastric mucosa.

No. 33.—Author's case. Male, aged nine months; painless intestinal hæmorrhage for about thirty-two hours. Source of bleeding not ascertained: At operation a Meckel's diverticulum was found thirty-five centimetres above ileocecal valve. It was approxi-

mately six centimetres long, and the tip was free and nodular. It was excised, with recovery. *Histological Examination*.—Peptic ulcer with erosion of a vessel at margin of area of gastric and intestinal mucosa.

NOTE.—In the New England Journal of Medicine, vol. ccvi, No. 16, April 21, 1932, appeared a paper by Henry W. Hudson, Jr., and Lewis Henry Koplik, entitled "Meckel's Diverticulum in Children; A Clinical and Pathological Study," with a report of thirty-two cases from the Children's and Infant's Hospital of Boston.

This paper appeared just after our paper was completed, and too late for inclusion of any of its cases in our analysis.

We feel that reference should be made to this paper, since, in the thirty-two cases reported, hæmorrhage was the chief symptom in seven instances and was noted in ten other instances.

This is a vastly larger number than has ever been observed in any other clinic.

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HÆMORRHAGE FROM MECKEL'S DIVERTICULUM

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DISCUSSION.—DR. J. M. T. FINNEY (Baltimore, Md.) said that his interest in Meckel's diverticulum began early in his surgical career: The first case of supposed appendicitis that he operated upon turned out to be a perforated Meckel's diverticulum. He reported a case in which, while they were not able positively to demonstrate the presence of gastric mucosa, the clinical history and findings strongly suggested a Meckel's diverticulum as the origin of the trouble. The tumor was about the size and shape of a Bartlett pear, situated about three feet from the ileocecal valve. It was largely cystic but contained an area which was definitely myomatous and which was continuous with the lumen of the bowel. There was considerable clotted blood surrounding the myoma, and here and there areas of scar tissue in the cyst wall. The cyst contained thin chocolate-colored fluid. The inner surface of the cyst wall was ulcerated, with areas of aberrant mucosa scattered here and there, but no gastric mucosa could be demonstrated. The pathological report was myoma of the ileum accompanied by cystic formation.

The patient was a man twenty-nine years of age with a history of three or four years' duration of recurrent hæmorrhages from the bowel. These were at times quite severe and would come on without warning. The blood was of rather tarry consistency, suggesting that the origin of the hæmorrhages was some distance up. There was little or no gastric disturbance. Slight indigestion was noticed from time to time, but no pain and no loss of weight. He had been actively at work right along. He had a congenital club-foot.

He had visited a number of clinics and had been seen by a good many physicians. In one of the well-known clinics, he spent four or five weeks on a Sippy diet to relieve his hæmorrhage. He had several transfusions, and was finally operated upon. The tentative diagnosis was "bleeding duodenal ulcer." Although no ulcer was found at the time of operation, a gastroenterostomy was done, hoping thereby to relieve the hæmorrhage. Following the operation, no improvement was noted. Finally, he came into our hands. After a careful and prolonged study, we were unable to make a positive diagnosis.

An incision was made in the upper part of the right rectus. Careful inspection of the abdominal cavity revealed no ulcer or scar. The gastroenterostomy opening was patent and there was no evidence of marginal ulcer. He had a definitely thickened appendix. This was removed. A thorough search of the abdomen was then made and a mass about the size of a small fist found on the floor of the pelvis, quite adherent to the bladder and large intestine. It was evident that another incision would have to be made in order to remove the growth. This was deferred to a second sitting. After three weeks, the abdomen was reopened in the mid-line below the umbilicus; the exposed tumor could be separated quite satisfactorily from the attached bladder and sigmoid, and out of the abdomen, and was resected.

The patient made a prompt and satisfactory recovery.

DR. EMIL GOETSCH (Brooklyn, N. Y.) referred to the case of a young man, nineteen years of age, who was admitted to the Bingham Hospital, Boston, because of intestinal obstruction. He had been operated on six years previously in Ireland for what was called an "abdominal abscess." The reporter presented three illustrations to show the pathology of the instances of aberrant gastric mucosa in Meckel's diverticulum. In the first one is a diagrammatic representation of the condition found at operation. A scar was present above the umbilicus as a result of the former operation. A mass of small intestine was found hanging over a band attached to the abdominal scar and continuous with Meckel's diverticulum, the whole cord being five or six inches in length. There was a small bowel obstruction. The cord was excised together with the diverticulum and the patient made an uneventful recovery. The diverticulum was opened. In the distal one-fourth of the diverticulum was a very thick mucosa which had a granular and papillary appearance, and a proximal thin mucosa of the type of the ileum.

Subsequent histological examination at the point representing a section through the transition zone was a thick gastric mucosa with large branching papillary glands and

HÆMORRHAGE FROM MECKEL'S DIVERTICULUM

the proximal ileal type of mucosa with the simple glands characteristic of the ileum. A high-power drawing of an actual section showed papillary columnar epithelium on the surface and long, deep glandular tubules reaching down to the submucosa, typical of the fundus area of the stomach.

On further magnification the surface type of goblet mucus cell, and in the neck of these glands, which are typical of the fundus of the stomach, are the two types of glandular epithelium, the chief or peptic cells bordering the lumen and the large parietal cells containing the typical acidophilic granules. Next we have a highly magnified section of the gastric mucosa showing eosinophilic granules in the parietal cells, and the chief cells with their basophilic secretion granules, typical of the gastric mucous membrane. The proximal mucosa resembles that of the duodenum except that there are no Brunner's glands. Further sections, in the oil immersion, high magnification, show the parietal cells, the large clear cells of the acid type containing eosinophilic granules, and the basophilic zymogenic secretion granules of the chief cells (acid-fuchsin methyl green method).

It was shown in the report to which I have referred and which was published in the Johns Hopkins Bulletin in 1919 that aberrant gastric mucosa, typical of the fundus area of the stomach, may occur in Meckel's diverticulum. Doctor Mason has called attention to the occurrence of ulceration, with consequent hæmorrhage, in this foreign tissue. In Doctor Goetsch's case such an ulceration subsequently perforated and gave rise to the abscess for which the man was operated upon six years previous to the exploration for intestinal obstruction. At this second operation, a Meckel's diverticulum with the curious findings described was removed.

DR. HUBERT A. ROYSTER (Raleigh, N. C.) reported the case of a boy about ten years of age who was seized with a sudden abdominal pain followed by hæmorrhage from the bowel. He had a very free discharge from both ears, which showed on examination diphtheritic organisms. Upon using the diphtheria antitoxin, this hæmorrhage ceased. He went away to another city for the treatment of his ears and was not seen by Doctor Royster for two months, when examination showed a nodule about the size of a thumb-nail in the lower abdominal region in the median line and one in the upper, which was a ventral hernia with omentum. The question was, that if the one above was a hernia, what was the other one below? In a few days the mass below began to enlarge and perforated through the abdominal wall before operation was allowed. At operation Doctor Royster opened the area below and drained it and a month later went in and explored and found a perforated Meckel's diverticulum showing gastric mucosa.

DR. VERNON C. DAVID (Chicago) agreed with Doctor Finney that patients, especially children, who are suspected to be bleeding from Meckel's diverticula should be carefully regarded from the standpoint of hæmorrhage from more common and less popularly discussed sources, papillomata, adenomata, and mild, low-grade ulcerative colitis. These things are rather common in children and may be without any symptoms whatsoever except the bleeding. He had happened to have seen quite a few instances of such conditions, some of whom had diagnoses of diverticulum of Meckel. He added the report of a case, a man thirty years of age, who was received into the hospital because of two or three very severe hæmorrhages which had reduced his hæmoglobin to thirty. The night of his entrance to the hospital, he began to have abdominal pain and after a transfusion because of very severe anæmia, which was increasing, was operated upon because of the pain, rigidity, temperature, and vomiting. No lesion was found in the duodenum or stomach. Deep in the abdomen was a tumor which was a Meckel's diverticulum in its outline, position, and shape, which had a perforation about the size of a dime. There were several nodules around it about the size of a pea and some enlarged mesentery glands which were hard; apparently the lesion was a perforated carcinomatous ulcer of Meckel's diverticulum. The specimen was lost so that

no microscopical examination was made—a bowel resection was done from which an uneventful recovery followed.

DR. EDWIN BEER (New York City) remarked that these ulcerations in Meckel's diverticulum may throw some light on secondary ulcerations following gastroenterostomy. He had seen a number of cases of aberrant gastric mucosa in Meckel's diverticulum. The literature of this subject, as well as the specimens examined pathologically, show the ulcer always at the periphery of the gastric mucosa; in other words, it is always at the place where the two mucosæ come together.

Is it an ulceration of ileac mucosa or is it an ulceration of the gastric mucosa? If it were an ulceration of the gastric mucosa, one would expect much more extensive destruction of the gastric mucosa, suggesting that it is probably an ulceration of the ileac mucosa. Perhaps secondary ulcers after gastrojejunostomy owe their origin to similar or analogous conditions. Misplaced gastric mucosa in the navel also is liable to produce a somewhat similar ulceration.

CLINICAL ASPECTS AND TREATMENT OF PRIMARY LYMPHOSARCOMA OF THE STOMACH AND INTESTINES

By DAVID CHEEVER, M.D.

OF BOSTON, MASS.

MALIGNANT neoplasms derived from other tissues than epithelium and affecting the gastro-intestinal tract are, it is true, relatively uncommon, but their occasional occurrence and serious prognosis warrant their study with a view to standardizing so far as possible the methods of treatment. Data from the literature are in a chaotic state, largely because of confusion and looseness in the classification of lesions, whose clinical courses vary greatly according to their type, so that the symptomatology, prognosis and reaction to treatment of one case may have but little resemblance to another, though they are designated by the same name. On account of the rarity of these conditions the experience of any one observer is limited, and the literature therefore consists largely of the recital of single cases, and makes but dull reading.

These tumors, usually loosely included under the term sarcoma, comprise a group sharply demarked in theory from the recognized epithelial tumors, but nevertheless not always clearly defined, since the embryonal origin of the cells of some, such as the endotheliomas, are still the subject of dispute. Moreover, in the case of certain small round-cell tumors, competent pathologists may differ about the classification as between carcinoma or sarcoma. Any of the mature mesoblastic tissues represented in the structure of the gastro-intestinal tract may be the seat of a malignant tumor, which then may be appropriately designated as fibro-, angio-, lipo-, myo-, myxo- and lymphosarcoma, respectively, according to the differentiated type of cell from which it springs. The designation of the tumor according to the morphology of its cells—whether composed of spindle, round or giant cells is not of much significance, since each of these types may occur in tumors springing from any of the mesoblastic tissues; on the other hand, it will be understood that the study of the cellular morphology is necessary for histological diagnosis.

According to Ewing,¹ sarcomas of the gastro-intestinal tract are of three chief groups: (1) Spindle-cell myosarcoma, which are likely to be bulky, more or less pedunculated growths, projecting either within the lumen of the viscus or into the peritoneal cavity, non-infiltrating, late in metastasizing, and apt to become cystic when growth has out-stripped the blood supply; (2) a miscellaneous group of round-cell or mixed-cell alveolar sarcomas, rare and not deserving of classification as a separate variety; (3) lymphosarcoma, which constitutes by far the most numerous and important group, and which requires most careful analysis, on account of the very numerous conditions

which cause hyperplasia of lymphoid tissue. Ewing states that tumors of lymphoid tissue may arise from any of its three normal components: lymphocytes, reticulum and endothelium. Lymphocytic hyperplasia gives rise to a lymphocytoma, which may be due to some irritant, bacterial or otherwise, especially the tubercle bacillus (simple or tuberculous lymphoma), or may be a part of the clinical syndrome known as lymphatic leukemia or pseudo-leukemia, or may be an independent, locally arising tumor having all the characteristics of malignancy—a true malignant lymphocytoma. Reticulum cells undergoing hyperplasia may form tumors which are a local manifestation of myeloid leukemia, or Hodgkin's disease, or may constitute an independent, locally arising malignant tumor which may be designated as large round-cell lymphosarcoma; finally, endothelial cells of lymphoid tissue may proliferate and cause the endothelial hyperplasia of tuberculosis, or a true tumor growth designated as endothelioma. When it is realized that many observers believe that Hodgkin's disease is due to an infection, probably with the tubercle bacillus; that apparently true lymphocytomas have been described in the course of the disease, and that on the other hand in patients with lymphocytoma an excess of lymphocytes similar in all respects to the tumor-cells has appeared in the blood, thus simulating leukemia, it will be realized how difficult and confused is the classification. Mallory² prefers to simplify matters by using the term lymphoblastoma to include all lesions variously spoken of as lymphocytoma, lymphoma, lymphosarcoma, pseudo-leukemia, lymphatic leukemia and Hodgkin's disease, believing that these are but different manifestations of the same underlying process. He defines the lymphoblastoma as a tumor of mesenchymal origin of which the cells tend to differentiate into lymphocytes—the type cell is the lymphoblast, which occurs abundantly in the generative centres in the lymph nodules of lymph-nodes, tonsils, gastro-intestinal tract and spleen. Minot and Isaacs,³ after referring to the utter confusion in the classification of diseases which have progressive enlargement of the lymphoid tissues as their most prominent feature, suggest the wisdom of recognizing four types depending on age incidence, clinical features, blood picture and pathological histology, as follows: (1) lymphatic leukemia; (2) pseudo- or aleukemic lymphatic leukemia; (3) Hodgkin's disease; (4) lymphoblastoma, having a distinct tendency to invade tissues, to involve tonsils, gastro-intestinal tract and serous membranes, and showing the multiplication of reticulum tissues and lymphoid cells usually called lymphosarcoma.

Whatever the inter-relation of these conditions, and the embryonal or adult origin of their characteristic cells, certain it is that a malignant tumor of lymphoid tissue may appear as an original focus in the gastro-intestinal tract, invade and destroy the structure in which it arises, spread by permeation and by lymphatic and blood metastasis, without the accompaniment of a blood dyscrasia such as lymphatic leukemia, and without the involvement of other lymphoid structures as in pseudo-leukemia, general lymphomatosis or Hodgkin's disease. Such a primarily local, but ultimately invading and

PRIMARY LYMPHOSARCOMA OF STOMACH AND INTESTINES

metastasizing malignant tumor closely corresponds to carcinoma in its clinical course, and is theoretically as susceptible of cure by extirpation. It apparently differs from carcinoma, as will be seen, in its markedly greater radio-sensitivity. In spite of theoretical objections the term "lymphosarcoma" conveniently designates these tumors.

This paper attempts to analyze the lymphosarcomas of the gastro-intestinal tract, excluding the rectum, which have been observed at the Peter Bent Brigham Hospital, Boston, since its foundation in 1913.* The diagnosis appears (with the variation "lymphoblastoma" or "malignant lymphoma") twenty-two times, but in four of these instances it is presumptive only, unconfirmed by biopsy or autopsy, while in a fifth a careful review of the histology has convinced the pathologist† that the tumor is in fact a small round-cell carcinoma. A sixth case is that of a fifty-one-year-old woman who died of septicæmia, whose stomach showed at autopsy a small, encapsulated, clinically benign nodule, whose histology was consistent with lymphosarcoma, and was so diagnosed. It seemed possible that a chance discovery at autopsy had revealed a malignant tumor at its early and still benign incipency. Further pathological study in the course of the preparation of this paper has led to the conclusion that it is a congenital tissue defect, of the type of lymphangioma, and non-malignant in character.

There remain, then, sixteen certified instances of primary lymphosarcoma of the stomach and intestines occurring in a hospital of 240 beds during nineteen years, in the course of which the total number of patients admitted for all tumors of the stomach and intestines was 976, giving a percentage of sarcomas of 1.63. Of the sixteen cases, nine were of the stomach; which among a total of 628 gastric tumors gives a percentage of lymphosarcoma of 1.4; seven were of the intestines, constituting 2 per cent. of all intestinal tumors. These figures correspond with most statements in the literature, that from 0.5 per cent. to 3 per cent. of all tumors of the stomach are sarcomas.⁴ Since the jejunum and especially the ileum are the most common situation of intestinal lymphosarcoma, which is much less common in the colon, and since carcinoma—while common in the colon—is exceedingly rare in the jejuno-ileum, it follows that lymphosarcoma of the small intestine, while rare, is by far the most common malignant tumor of that portion of the alimentary tract. Its frequency of incidence seems to increase with its distance from the stomach, being most uncommon in the duodenum and most frequent in the terminal ileum, where it naturally often involves the cæcum. In the Brigham Hospital series of seven cases, the disease was located in the jejunum in two instances, in the jejuno-ileum in two instances,

* For reference, the patients on whom this paper is based are numbered as follows in the Peter Bent Brigham Hospital records: S-3401; S-7322; S-13985; S-14572; S-14737; S-18055; S-21507; S-24969; S-24796; S-26974; S-31823; S-35035; S-38857; M-7428; M-17127; M-19182.

† Dr. S. Burt Wolbach has kindly reviewed the pathological material and his assistance is acknowledged by the writer.

in the distal ileum in two cases, and in the terminal ileum with involvement of the cæcum in one case. There was no instance of primary location in the colon.

Since the etiology is absolutely unknown, there is no object in rehearsing the familiar speculations regarding it. There was nothing to throw light on it derived from the study of this series.

Sex seemed to play no part in the incidence, there being four males and five females among the gastric cases, and four males and three females among the intestinal. The average age of all patients was 53.5 years; the youngest was thirty, the oldest seventy-five; the gastric cases averaged 56.2 years and the intestinal 50.1. This is apparently somewhat at variance with common experience, which indicates that sarcoma of the gastro-intestinal tract occurs at an age averaging at least ten years earlier. Balfour and McCann,⁵ reporting forty-five cases of sarcoma of the stomach, give the average age as forty-three years, and the preponderance of males over females as more than 2 to 1. Douglas,⁶ analyzing the literature, gives the average age as 41.6, and the sexes equally affected. Haggard⁷ quotes the average age as about 45.8 years and D'Aunoy and Zoeller⁸ tabulate 135 scattered cases whose ages average 36.7 years, with males almost twice as numerous as females. Sarcoma in general is widely recognized as much more prevalent in youth than is carcinoma, and the literature of sarcoma of the gastro-intestinal tract reveals the general opinion that it occurs on the average at a considerably earlier age than does carcinoma—a belief which does not seem to be sustained by the Brigham Hospital series.

Primary lymphosarcoma of the gastro-intestinal tract may have its origin in any nidus of lymphoid tissue, but appears most often to begin in a lymphoid follicle of the submucosa, whence it spreads by permeation along tissue spaces, and by infiltration through the various layers of the viscus, especially the muscularis. Since it does not at first involve the mucosa, ulceration is neither an early nor a characteristic occurrence, in sharp distinction from carcinoma. It has little tendency to penetrate the serosa until late in the disease, when perforation due to ischæmic necrosis is not uncommon. Since the tumor-cells lie in a scanty and very delicate reticulum, instead of being accompanied by the definite and important framework of connective-tissue stroma usually characterizing carcinoma, there is but little tendency for the neoplasm to contract and constrict the visceral lumen; rather does it seem to separate and thus weaken the fibres of the muscularis, or perhaps paralyzes the intrinsic neuromuscular mechanism, so that the viscus, especially if it be the intestine, appears dilated rather than contracted. The infiltrating lymphosarcoma under consideration does not develop the massive semi-pedunculated growths projecting either into the peritoneal or the visceral cavities. Metastasis may be by both blood- and lymph-streams—indeed, the involvement of regional lymph-nodes may be both early and extremely extensive, so that the masses of tumor-nodes in the mesentery or retroperitoneal tissues may quite overshadow the primary growth. Perusal of the literature

PRIMARY LYMPHOSARCOMA OF STOMACH AND INTESTINES

reveals much difference of opinion on this point, due usually to confusion of various other histological types with true lymphosarcoma, since it is well known that sarcoma in general, being built on an architecture of new blood-vessels, and perhaps devoid of lymphatics, is much more prone to metastasize by the blood than by the lymph currents. The primary lymph-node invasion is almost certainly by direct permeation rather than by free-cell metastasis. Blood metastases are necessarily through the portal system to the liver.

In gross appearance lymphosarcoma of the stomach cannot be differentiated from carcinoma, especially of the infiltrating "linitis plastica" type. There is diffuse thickening of the wall, of rubber-like consistency, usually without sharp delimitation, often purplish in color and contrasting with carcinoma simplex and malignant adeno-carcinoma by its softer consistency and lack of nodularity. The regional nodes, if involved, are large, smooth, elastic rather than hard, apt to be matted together and to form a tumor mass along the curvatures not separable from the parent tumor. The cut surface is of a uniform grayish or grayish-pink color, without gross evidence of structure. These gross characteristics are not sufficiently distinctive to permit certain differentiation from carcinoma. In the intestine the appearances are similar, the gut appearing enlarged and dilated, and the thickened rubber-like wall justifying the comparison with a piece of garden hose, an appearance quite different from the characteristic sharply delimited annular constricting appearance of the typical scirrhus adeno-carcinoma of the colon. In the cæcum, however, the gross appearances are again very similar to carcinoma. Microscopically, the tumors are composed of varying sizes of small or large lymphocytes, round, oval or polyhedral, with round, sharply outlined nucleus containing chromatin granules often peripherally distributed, scanty, basophilic cytoplasm, and delicate, sometimes scarcely demonstrable reticulum without definite structural arrangement, except for the appearance of thin-walled blood-vessels invaded by tumor-cells. Mitoses are usually numerous and often quite irregular. In some instances the differential diagnosis is scarcely to be made between lymphocytoma and a rapidly growing small round-cell carcinoma, unless secretory vacuoles in the cells of the latter can be demonstrated, and it is undoubted that many cases are reported as lymphosarcomas which are in reality carcinomas.

For reasons related no less to treatment than to the perfection of diagnostic science it would be highly desirable to be able to distinguish clinically between lymphosarcoma and carcinoma of the gastro-intestinal tract. All authorities agree that in the case of the stomach this is usually impossible. Cutler and Smith,⁹ reporting in 1922 two instances of lymphoblastoma of the stomach (which are included in the present Brigham Hospital series) state that differential diagnosis is impossible. D'Aunoy and Zoeller⁸ stated in 1930 that no case is on record where a clinical diagnosis was established. Pemberton¹⁰ says there is no record of a pre-operative diagnosis. Ruggles and Stone¹¹ say that X-ray findings are not sufficiently characteristic to permit of a specific diagnosis of lymphoblastoma. Balfour and McCann,⁵ report-

ing forty-five cases of proved sarcoma of the stomach occurring at The Mayo Clinic between January, 1908, and July, 1929, say that two were diagnosed before operation as sarcoma, and that in one of these the X-ray diagnosis of lymphosarcoma was correctly made. Presumably the other was some other form of sarcoma, such as myosarcoma, which, in contrast to lymphosarcoma, may present features permitting presumptive diagnosis.

Analysis of the symptoms of the patients in the Brigham Hospital series with involvement of the stomach showed that all complained of abdominal—usually epigastric, pain or discomfort, while some stressed such symptoms as anorexia, dyspnoea, and loss of weight, during a period varying from two weeks to two years before admission to the hospital. The average duration of symptoms was about seven months. Five of the nine cases complained of vomiting, but never of gross blood. Gastric analysis was done in five cases, all but one of which showed low or absent acid values. Occult blood was noted but once. No tarry stools were reported, but tests were positive for occult blood in four of the five cases in which the test was done. An epigastric tumor was felt in seven cases. X-ray examination was made in six instances, in four of which a filling defect was noted, and in two the crater of an ulcer. In one a 100 per cent. six-hour barium residue was reported, and in two a 20 per cent. and a 25 per cent. respectively. The tentative diagnosis was carcinoma in six, ulcer in one, malignancy of the abdomen in one. In all patients but one there was a mild to moderate secondary anaemia.

From this analysis it appears that the typical picture of a patient with lymphosarcoma of the stomach is an individual in the sixth decade, who has complained for seven months more or less of epigastric discomfort or pain, indigestion, moderate loss of weight and strength, and often vomiting. Examination shows an epigastric tumor and moderate anaemia; X-ray shows a filling defect with or without stasis, sometimes with a crater. Gastric analysis shows usually a low or absent hydrochloric acid and occasionally traces of blood. The stools usually show occult blood. It cannot be denied that this description fits perfectly a typical case of gastric carcinoma. Holmes, Dresser, and Camp¹² report X-ray studies of eight cases of lymphoblastoma of the stomach observed at the Massachusetts General Hospital, of which five appear to be true primary lymphosarcoma of the type now under consideration. No correct diagnosis was made in these cases and the authors conclude that the X-ray appearances do not differ from carcinoma except that peristalsis does not seem to be interfered with so much.

Analysis of the symptomatology of the seven cases of lymphosarcoma of the intestine constituting the Brigham Hospital series indicates that the duration of symptoms before admission varied from three weeks to seventeen months, with an average period of six and one-half months. The chief complaint in every case was abdominal pain, noted as epigastric in two instances; subsidiary complaints were vomiting and constipation, each in two instances. All these patients had lost from twenty to thirty pounds in weight. Stools

PRIMARY LYMPHOSARCOMA OF STOMACH AND INTESTINES

were noted as bloody by one patient, as tarry by one other. In every instance but one a tumor could be felt. In the four cases in which gastric analysis was done, free hydrochloric acid was absent. X-ray examination was made in six instances and was reported as follows: (1) residue in ileal loops; (2) 100 per cent. gastric residue and dilated duodenum; (3) rigidity of ileocecal valve and slight filling defect of the cæcum; (4) distension and obstruction of the small intestine; (5) filling defect of the sigmoid, not characteristic; (6) filling defect of the cæcum. As already noted, the nature of the infiltrating, non-constricting pathological process is such as not to lead to mechanical obstruction, so that such a picture as is given by the annular constricting carcinoma of the colon is not afforded. The filling defects noted are usually due to extrinsic pressure from large masses of metastatic glands. All patients but one showed a slight or moderate secondary anæmia.

The average clinical picture of a patient with lymphosarcoma of the intestine may be described as follows: a middle-aged or possibly much younger individual who for some months has complained of abdominal pain, situated anywhere but often epigastric, not definitely related to food or bowel action, sometimes but not necessarily accompanied by vomiting; an anæmia of secondary type with otherwise normal blood-picture; an insensitive mass anywhere in the abdomen, either occult or gross blood in the stools, and by X-ray either no striking appearance, or some evidence of dilated loops of small intestine with tendency to local stasis of the barium. An opaque enema would be likely to show a filling defect or deformity, if the disease were located in the colon.

The treatment of lymphosarcoma of the stomach or intestine, until the advent of therapeutic radiation, was exactly as in carcinoma—by an attempt at radical extirpation, and the results have been such as to inspire widespread pessimism. The classic case of Ruppert¹³ is widely quoted as the longest reported survival. His patient was a woman of fifty-eight years whose stomach was almost entirely involved in a primary lymphosarcoma accompanied by numerous nut-sized glands in both omenta; a subtotal gastrectomy was done and the patient was reported as living without evidence of recurrence fourteen and one-half years later. In making his report in 1912 Ruppert said that medical literature revealed but twelve radical operations for gastric lymphosarcoma, of which but seven made an operative recovery. The next longest survival, nine years, appears to be that of Finsterer (quoted by D'Aunoy and Zoeller.⁸ Balfour and McCann's series⁵ of forty-five cases of all types of sarcoma of the stomach afforded thirty-eight resections which survived operation; of those living when last heard from the average duration of life was five years, the longest nine years. This list, however, includes types other than lymphosarcoma. Isolated or small groups of cases are reported with survivals for lesser periods. Approximately the same results have followed surgical extirpation of the disease affecting the intestinal tract. Rankin and Chumley¹⁴ reporting in 1929 eighteen instances of lymphosarcoma of the colon including the rectum, noted

fifteen radical resections⁸ with four operative deaths; in five patients the disease recurred, and the remaining six were alive and well for four years and three years and various lesser periods. Weeden,¹⁵ reporting in 1929 twelve cases of lymphosarcoma of the intestine from the New York Hospital, noted six resections with three post-operative deaths, and survival periods of three and one-half years and one year for the two patients who were traced. Graves¹⁶ reports three cases resected with a maximum survival of three years without recurrence. Loria,¹⁷ in 1925, reviewed all reported cases and stated that the prognosis was very poor; he quotes Cornier and Fairbanks¹⁸ as analyzing ninety-six cases, with only one patient surviving as long as eight years. There are numerous isolated reports in the literature, which give the impression that on the whole the prognosis of the disease is even less favorable in the intestine than in the stomach.

The well-known radiosensitivity of undifferentiated cells in general and of lymphocytes and lymphoblasts in particular offers ground for hope that radiation may be effective in the relief of lymphosarcoma. Ruggles and Stone¹¹ say that X-ray therapy has a good deal to offer and on this account stress the desirability of diagnosis without exploratory operation, while regretfully admitting that it seems to be impossible. They present an analysis of eleven cases but do not mention the result of X-ray treatment. Matas, discussing a paper by Loria,¹⁷ stated in 1925 that deep X-ray therapy and radium have proved unavailing. Gunsett and Oberling¹⁹ report a remarkable case of a forty-eight-year-old man with an extensive annular neoplasm of the stomach, adherent to and involving the pancreas, extending upward on the lesser curvature to the cardia, with extensive glandular involvement along both curvatures—hopelessly inoperable. Biopsy of a gland showed lymphoblastic sarcoma; the cells were round or polyhedral with large nucleus containing one or two nucleoli and a delicate chromatin network, cytoplasm staining pink with eosin; mitoses were frequent and often irregular in type. The patient was given X-ray therapy in seventeen sessions during three weeks and at the end of five years was living and without symptoms if he avoided indigestible food; X-ray examination then showed that most of the stomach seemed to have disappeared! Strauss²⁰ reports the instance of a man of sixty-two with an inoperable tumor of the duodenum; biopsy showed lymphosarcoma. He received deep X-ray therapy and two years later had gained forty pounds, was in excellent health and showed no evidence of recurrence. Freeman²¹ reports a striking case of a man sixty years of age upon whom he performed resection of the stomach—the lines of section passing through tumor tissue. The pathological diagnosis was variously reported as carcinoma, lymphosarcoma, inflammatory tissue and chronic granuloma, but subsequently pathologists of The Mayo Clinic and Columbia University rendered a verdict of lymphosarcoma. The patient had X-ray treatment (inadequate on account of his objection) and small doses of Coley's fluid, and was reported as well eighteen months later—the stomach appearing normal by X-ray except for reduction in size.

PRIMARY LYMPHOSARCOMA OF STOMACH AND INTESTINES

The results of treatment in the Brigham Hospital series are as follows: of the nine cases of lymphosarcoma of the stomach two died on the medical service shortly after admission, and autopsy showed in each inoperable primary lymphosarcoma of the stomach with metastases, and with terminal perforation. Two patients were explored, found inoperable (one had perforative peritonitis) and died a post-operative death. One patient explored and found inoperable, made an operative recovery and died three months later after having been admitted for X-ray treatment to another hospital, whose records, however, fail to show whether she was treated or not. One patient, No. S-31823, a man of seventy-one, had an exploratory laparotomy which revealed a large tumor mass occupying most of the stomach and adherent to and involving the left lobe of the liver; he made an operative recovery and had two X-ray treatments before discharge; the tumor diminished rapidly in size but the general condition did not improve and he died four months later. The biopsy of this tumor showed it to be composed of rather large round cells containing large nuclei, a rim of dark-staining cytoplasm and many mitoses, and it was designated lymphoblastoma. One patient, No. S-38857, was explored, found inoperable, given X-ray treatment and restored to apparently perfect health. Her story will be examined presently. Only two patients could be subjected to radical resection—one (No. S-14572) operated on by Dr. E. C. Cutler in 1921, had a resection of the pyloric third of the stomach with tributary involved nodes, made a normal convalescence but died of recurrence one and one-half years later, without having had supplementary X-ray treatment; the other (No. S-21507) operated on by the writer in 1924, had a segmental resection of the middle third of the stomach for an ulcerated lesion of the posterior wall, made a good recovery and was given two X-ray treatments on discharge from the hospital, but failed to report for later therapy. Six years later she wrote that she was "in better health than for years and had no stomach symptoms." Since then it has been impossible to trace her. The histological structure of the tumor showed "lymphoid tissue infiltrating the connective tissue and smooth muscle of the muscularis mucosa and submucosa; the cells are of lymphoid type with round nucleus of sharp outline and peripherally distributed chromatin, the amount of cytoplasm is small; there are occasional larger cells with basic staining cytoplasm; the growth is distinctly invasive and could not be confused with inflammation; there are many mitoses; the diagnosis is lymphosarcoma." (S. B. Wolbach.)

The treatment of the seven patients with lymphosarcoma of the intestines constituting the Brigham Hospital series resulted as follows: one died on the medical service shortly after admission, of metastases and perforation; three had exploratory laparotomy (two with palliative anastomoses) for inoperable tumors with extensive glandular metastases, followed by X-ray treatment; these patients died after intervals of four, seven and ten months respectively; three patients had resection (two by Dr. John Homans and one by the writer) without mortality; one of these could not be traced after his discharge; one

died of recurrence about one and one-half years later, and the third patient lived in perfect health for more than four years and died of angina pectoris—his physician reporting that he noted a palpable mass in the abdomen. Neither of these cases had X-ray therapy.

The history of one patient may be given in more detail, since it seems to point the way to a rational treatment of these cases.

L. M. G., No. S-38857—a woman sixty-three years of age, previously well, had complained for two years of unaccountable anorexia, indigestion and occasional nausea, and for ten months of increasing epigastric discomfort, loss of weight, pallor, asthenia and occasional vomiting without blood. Examination showed a mass in the epigastrium; the blood showed hæmoglobin of 65 per cent., red cells 4,600,000, white cells 5,850 and

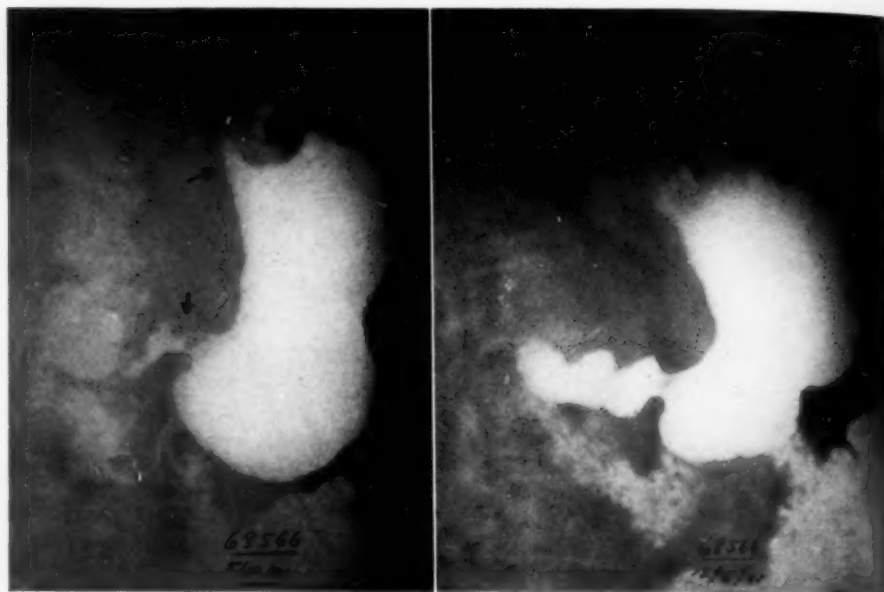


FIG. 1.

FIG. 2.

FIG. 1.—Before radiation. Note the extensive filling defect of the antrum, the rigid appearing and irregular lesser curvature, and the defect caused by extrinsic pressure near the cardia.

FIG. 2.—Seven and one-half months after radiation. Note the disappearance of the filling defect, the normal-appearing lesser curvature, and the absence of evidence of extrinsic pressure from masses of neoplastic glands.

normal cytology; X-ray (Fig. 1) showed an extensive filling defect of the pyloric antrum with rigidity of the whole lesser curvature, 25 per cent. six-hour residue, and evidence of extrinsic pressure near the cardia. No gastric analysis was made. The pre-operative diagnosis was carcinoma, probably inoperable. At operation by the writer on May 23, 1931, under avertin and supplementary ether anaesthesia, there was found an infiltrating tumor mass involving the whole antrum and the whole lesser curvature to the cardia; there was direct adhesion to and apparently involvement of the pancreas, and extensive glandular involvement along the lesser curvature with especially large masses about the cardia and celiac axis. The liver was uninvolved. Nothing unusual was noted about the tumor except that the diseased nodes were unusually large, rounded and elastic. Tissue was taken for immediate diagnosis and reported as probable small round-cell carcinoma. Convalescence was exceedingly stormy on account of inability to take nourishment and a moderate pneumonic or atelectatic complication. Paraffin sections of the tissue showed

PRIMARY LYMPHOSARCOMA OF STOMACH AND INTESTINES

"cells with scant basic cytoplasm whose boundaries are not distinct; there are many degenerating cells with small dense nuclei (pyknosis). There are many mitoses with peculiar dense, small, compact spindles of the nuclei; there are accompanying fibres simulating stroma formation but no arrangement into columns or glands and no secretory vacuoles are seen. The diagnosis is lymphosarcoma." (Figs. 3 and 4.)

X-ray treatment was begun on the fourteenth day. After a brief period of toxic manifestations necessitating mild and divided dosage, the response was most favorable, the nausea and vomiting ceased and nourishment began to be taken without discomfort. Six months later a barium X-ray (Fig. 2) showed complete disappearance of the filling defect of the stomach, including the evidence of extrinsic pressure from involved nodes near the cardia, the stasis had ceased, and no trace of a pathological process remained except a slight narrowing of the antrum as though by scar tissue. Fourteen months after the operation the patient writes that she has gained thirty pounds in weight, is

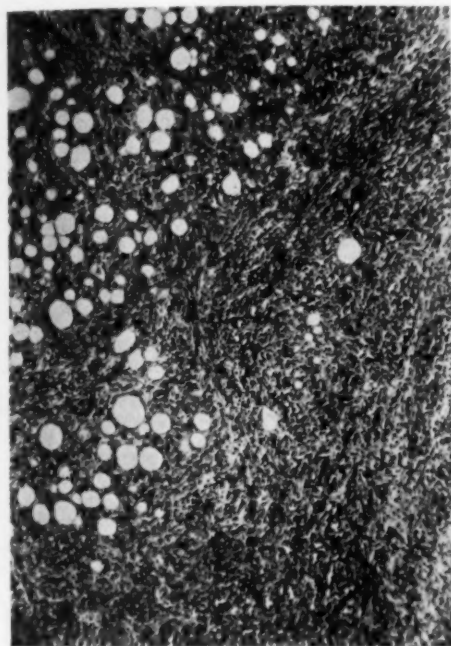


FIG. 3.

FIG. 3.—Tumor-cells invading fat tissue of the omentum, low power (magnification = 112).

Case No. S-38857.

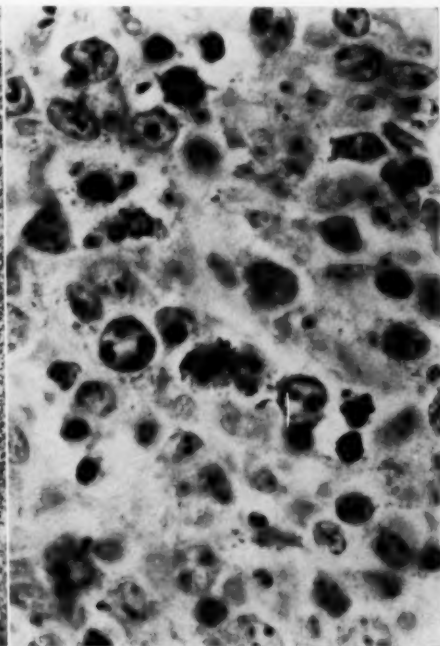


FIG. 4.

FIG. 4.—Tumor-cells; high power (magnification = 1500). Case No. S-38857.

regularly attending to her former clerical occupation, and is eating a liberal mixed diet without discomfort or symptoms of any sort.

Review of this material from the Brigham Hospital clinic confirms the general impression that lymphosarcoma of the gastro-intestinal tract is an uncommon condition and one carrying the gravest prognosis. It is as insidious as carcinoma, and seems to offer no greater probability of reaching the surgeon in an early and operable stage. In the stomach its radical operability is extremely low—in this series only 22.2 per cent., and its differential diagnosis from carcinoma, in the writer's opinion, absolutely defies the skill of the diagnostician, except in the rare instances where it occurs

in individuals so young that carcinoma would be a clinical curiosity. It is realized that these statements as to low rate of operability and gravity of prognosis are at considerable variance with views expressed by some authorities, but they are based on all the instances of the disease observed in a hospital of 240 beds during a period of nineteen and one-half years, on the medical and surgical services and in the autopsy room. In comparing the published evidence, the reader must again be warned as to the utter confusion which he will encounter, due to the failure of many writers to differentiate consistently or at all between the various types of "sarcoma" either in reporting their cases or in summarizing the literature, whereas, as has been noted, true lymphosarcoma differs widely in symptomatology, operability and prognosis from the fibro-, myo-, lipo-, myxo-, angio-sarcoma group—almost as widely, perhaps, as does true malignant osteogenic sarcoma of bone from giant-cell "sarcoma." When the intestine, especially the small bowel, is the seat of the disease, there appears to be probability of earlier diagnosis reflected in an operability in this series of 42.8 per cent., though the ultimate prognosis appears to be quite as grave as in the stomach.

Unless our conception of primary lymphosarcoma of stomach and intestine as originally a local disease is quite erroneous, radical cure by total extirpation is possible, and this should be the goal of general practitioner and surgeon alike, to be attained by early diagnosis and prompt operation. But it is amply evident that in therapeutic radiation we have a powerful substitute, if surgical removal is impossible, and in any case an important aid. Of the Brigham Hospital series, the gastric cases most benefited were No. S-21507, who had a resection followed by X-ray treatment and who reported herself six years later to be in perfect health, and No. S-38857 who had X-ray therapy for an inoperable lesion and who shows no clinical evidence of the disease after fourteen months, whereas No. S-14572—an apparently favorable case, had a resection without X-ray therapy and died of recurrence in eighteen months. An unfavorable result, but one in whom not much could be expected, was No. S-31823, an old man with extensive involvement of the liver, who lived but four months after exploration and X-ray treatment. The intestinal cases do not permit of dependable deductions; three very advanced inoperable cases who had X-ray were possibly benefited, and two patients with resection but without X-ray died with evidence of recurrence after one and one-half and four years. It may be believed that they would have survived longer if they had had the benefit of X-ray therapy.

In conclusion, the writer, on the strength of this survey of a group of patients with lymphosarcoma of the gastro-intestinal tract, wishes to urge the importance of exploratory operation and biopsy even in patients where the clinical evidence points strongly to inoperability, in order that the occasional case of lymphosarcoma may be identified and receive the benefit of X-ray therapy. It may be objected that this is unnecessary since radiation may be used in any event as a therapeutic test; the drawback to this plan is the usually uncomfortable and sometimes serious reaction of a debilitated patient

PRIMARY LYMPHOSARCOMA OF STOMACH AND INTESTINES

to X-ray therapy, but above all it seems important that adequate evidence should be accumulated as to the exact histological type of neoplasm which can be benefited by this means.

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THE FATE OF THE OBSTRUCTED LOOP IN INTESTINAL OBSTRUCTION FOLLOWING AN ANASTOMOSIS AROUND THE OBSTRUCTION WITHOUT RESECTION

BY WILLIAM L. ESTES, JR., M.D., AND C. E. HOLM, M.D.

OF BETHLEHEM, PA.

WHEN intestinal obstruction is found to be due to a mass of small intestinal adhesions without gangrene or hernia, and the patient's condition justifies radical surgery, often the best procedure to relieve the obstruction is an entero-anastomosis around the adherent coils, a jejunostomy, ileo-ileostomy, or ileocolostomy with or without an enterostomy. In fact, entero-anastomosis has been urged as superior to enterostomy in the treatment of intestinal obstruction (Vaughan). In properly chosen cases an uneventful recovery usually follows this operation with complete relief of symptoms and subsequent good health, as the following cases demonstrate:

CASE I.—Male, aged forty-one years. Six months before he had had a cholecystectomy and appendectomy elsewhere. Normal recovery and good health except for constipation until five days before admission when symptoms of intestinal obstruction supervened, culminating in severe abdominal cramps with fecal vomit the day of admission. Immediate operation revealed a dense mass of small intestines adherent to the parietal peritoneum, to the base of the mesentery and to the cecum in the right lower abdomen. One band of adhesions had formed a small orifice through which had prolapsed a coil of ileum which had become obstructed. This adhesion was freed and the obstruction released, but the remaining matted mass of intestine seemed so likely to obstruct again that an ileo-ileostomy around this area was rapidly done. The patient made an uneventful recovery save for the development of a small ischio-rectal abscess. Examination three years later disclosed occasional slight constipation. No diarrhoea. Patient completely relieved, but still below weight.

CASE II.—Woman, aged forty-five years. Admitted April 5, 1930. She had in 1914 a bilateral oöphorosalphingectomy and appendectomy, tonsillectomy in 1920, hemorrhoidectomy in 1922. For six or seven years she has had intermittent acute cramps in lower left abdomen about every three or four weeks. Very brief duration. These were unrelieved by an operation in 1925 when omental adhesions were released. She had been markedly constipated and had noticed for three weeks a fullness in the lower left abdomen. Two days after admission to the hospital she developed a definite intestinal obstruction.

At operation, a mass of pelvic adhesions was found comprising most of the ileum, sigmoid, omentum, and transverse colon, evidently causing obstruction in the ileum. Adhesions of the transverse colon were freed and a lateral anastomosis was made from a point in the small intestine above the adhesions to the middle of the ascending colon—ileocolostomy. Recovery uneventful. Bowels moved spontaneously. Pain relieved.

Report two years later shows patient completely well. She has occasional constipation and no other intestinal symptoms since operation except belching of gas.

Summary.—Two cases in which entero-anastomosis was done for ileus due to massive intestinal adhesions had an uneventful convalescence and have remained well for two to three years after operation.

OBSTRUCTED LOOP IN INTESTINAL OBSTRUCTION

However, in the following cases a similar lateral anastomosis was done but a rather remarkable post-operative complication was encountered.

CASE III.—Male, aged twelve years. Admitted June 11, 1929. Three days before admission, the patient was seized with acute appendicitis, and at operation one hour after admission a gangrenous, perforated appendix was found within a large abscess walled off by intestinal coils. Appendectomy was done and the abscess drained. Convalescence was prolonged because of wound infection, but was otherwise uneventful. At a follow-up examination October 17, 1929, the patient was in excellent health. He remained free from abdominal symptoms until April 5, 1930, when intestinal obstruction occurred. At operation the terminal three feet of ileum was found adherent to itself, to the cæcum, and to the anterior abdominal wall. Adhesions were divided to release a three-inch loop of strangulated but viable ileum. Inasmuch as extensive, dense adhesions threatened future strangulation, a lateral anastomosis was established between the transverse colon and the ileum at a point proximal to the adhesions. Throughout the convalescent period, the patient had a good appetite and his general condition was excellent. A mild, painless diarrhœa, with considerable borborygmus and moderate distension of the lower abdomen developed one week before his discharge on April 22, continued in a mild form until May 4 when the diarrhœa became severe and painful, and vomiting occurred. These symptoms became progressively worse, and at readmission on May 9 the patient was undernourished, dehydrated, drowsy, and very toxic. The abdomen was moderately distended and generally tender, but there was neither rigidity nor palpable mass. At operation the following morning, the terminal three feet of ileum side-tracked on April 7 were found elongated to seven feet, greatly dilated, acutely inflamed and ulcerated, with the distal one foot completely obstructed in a mass of adhesions. The meso-ileum contained many lymph-nodes varying in size from a pea to a walnut. The colon was collapsed proximal and distal to the anastomosis. The side-tracked loop was resected from the anastomosis to the cæcum. During the manipulations of resection, several ulcerations of the loop perforated. The abdominal cavity was drained. A serious wound infection and the pre-operative debility prolonged the convalescence. A mild diarrhœa persisted throughout the patient's stay in the hospital and continued for several months after his discharge. Recuperation was slow for several months following his return home, but at the last follow-up examination one year later, May, 1931, he had gained twenty-five pounds in weight and his general health was excellent.

Summary.—A boy, aged twelve, nine months after an appendectomy and drainage of an appendiceal abscess, developed an intestinal obstruction due to massive post-operative adhesions of the ileum which was relieved by an ileocolostomy around the obstructing coils. Post-operative diarrhœa supervened with low abdominal pain and distention and borborygmus which failed to respond to treatment. One month later re-operation was necessary. The terminal side-tracked ileum was found to be a hugely distended mass of adherent intestinal coils, ulcerated, acutely inflamed, and obstructed. Following resection of this ulcerated and obstructed mass, the patient made a slow but satisfactory recovery and has remained well ever since.

CASE IV.—Male, aged sixteen years. Admitted November 18, 1929, with symptoms and signs of acute intestinal obstruction of two days' duration. At operation several loops of terminal ileum were found matted together and adherent to the lateral wall of the pelvis, around a gangrenous Meckel's diverticulum, causing a complete intestinal obstruction. The involved loops of ileum with the Meckel's diverticulum were resected, following which a lateral anastomosis was performed between the ascending colon and the ileum, four inches proximal to the resection. The four-inch blind limb of ileum distal to the anastomosis was placed over the large defect in the posterior parietal peritoneum of the pelvis where the intestinal coils had been adherent. Ten days after the operation the patient became slightly distended, and began having mild attacks of visible

peristalsis in the lower abdomen which recurred during the remainder of his stay in the hospital. His general condition was good. After going home December 7, 1928, the attacks of visible peristalsis recurred with increasing frequency and were associated with marked borborygmus and pain. He had from two to six loose bowel movements daily, the pain being relieved shortly before defecation. His symptoms becoming progressively worse, he was readmitted January 26, 1929, and was operated upon two days later. The four inches of blind ileum distal to the anastomosis performed the previous November had become greatly elongated and distended, and filled the lower half of the abdominal cavity. It was coiled upon itself, with dense adhesions to the cæcum and pelvic wall. The blind end of the ileum was partially freed from adhesions when the patient's general condition became too serious to permit resection, and the operation was hastily terminated by performing a lateral ileo-ileostomy between a point near the end of the blind limb and an area immediately proximal to the former ileocolostomy. Recovery was prompt, and the patient was discharged February 9, 1929. *Examination* September 21, 1929, showed that the patient was much underweight, due to a severe diarrhœa of four months' duration. There had been occasional attacks of distension, borborygmus, and painful peristalsis. He was placed on a strict diet and January 2, 1930, was greatly improved, although abdominal distension and a mild diarrhœa had persisted. His appetite had been good throughout.

The patient was readmitted January 7, 1930, during an aggravation of the abdominal symptoms, and he was operated on three days later. The lower two-thirds of the abdominal cavity were filled with the hugely elongated and dilated blind loop of terminal ileum which was fully eighteen inches in length and three to four inches in diameter and showed marked ulceration throughout. The mesenteric lymph-glands were all markedly enlarged. Proximal to the ileocolostomy the ileum seemed normal. The blind loop of ileum was freed of adhesions and completely resected and the sigmoid sutured over the denuded areas. The patient was discharged January 28, greatly improved, although he still had a mild diarrhœa. The diarrhœa persisted for several weeks after his return home. Fifteen months later, he was in excellent health, had gained thirty-five pounds in weight and had no gastro-intestinal complaint.

Summary.—A boy of sixteen years, after resection of the terminal ileum, for intestinal obstruction due to a Meckel's diverticulum, and lateral ileocolostomy with a short loop of blind ileum left distal to the anastomosis, developed a severe enterocolitis with low abdominal distension, pain, and borborygmus and was only slightly relieved until a complete resection of the blind loop was finally performed, said loop having become hugely elongated, distended, and ulcerated, filling almost one-third of the abdomen. He has remained well.

Comment.—This fourth case has been cited because of its great similarity to the third, due to the ulceration and dilatation of the short blind end of ileum beyond the anastomosis which had been allowed to remain. In defense of leaving this small portion of blind ileum it should be stated that neither the omentum nor the sigmoid was available to cover the denuded pelvic wall. It was therefore feared that post-operative small intestinal adhesions might again produce obstruction. Hence, it was deliberately planned to use this blind end to cover over the raw area and to meet later any complications that might result from this procedure, in spite of the knowledge that elongated blind ends in lateral anastomosis are universally condemned.

Both these cases showed what seemed to be a similar clinical entity—a post-operative enterocolitis evidenced by diarrhœa, visible peristalsis, abdominal distension and colicky pain and borborygmus caused by stagnation, dila-

OBSTRUCTED LOOP IN INTESTINAL OBSTRUCTION

tation, and ulceration of an obstructed or blind loop of intestine, that required resection of the involved loop for cure, in spite of a fecal path around the obstruction.

A survey of recent literature fails to reveal any reference to ulcerative enteritis as a complication of entero-anastomosis for intestinal obstruction. Vaughan,* however, in arguing for entero-anastomosis as against enterostomy in ileus, has cited one case in which "symptoms were much improved by entero-anastomosis," but resection of the side-tracked intestine was necessary for complete relief; in another case, after the entero-anastomosis, recurring attacks of abdominal pain and vomiting persisted and resection of the adherent masses of small intestine was necessary in which "many obstructive points were encountered forming dilated bowel areas filled with fecal matter and pus." Three other of his cases remained well without requiring resection.

In view of the fact, therefore, that after entero-anastomosis certain cases recovered without post-operative untoward incident, and others required resection of the obstructed loops because of an ulcerative enteritis, it seemed worth while that one of us (C. E. H.), should attempt experimentally to produce a post-operative enteritis after a lateral anastomosis to ascertain why this complication arises.†

These experiments were carried out in the experimental surgical laboratory of the University of Pennsylvania through the courtesy of Dr. I. Raydin, whose kindness is hereby gratefully acknowledged.

It was surmised that the reason for this post-operative complication is that obstruction occurred or persisted in the side-tracked loop which caused stagnation, difficulty in emptying against the normal fecal current, and gradual dilatation and ulceration. When this loop remains unobstructed, convalescence is normal and the patient remains well.

It seemed essential to determine: (1) Is obstruction in the side-tracked loop after a lateral anastomosis the cause of the dilatation and ulcerative enteritis? (2) Does ulcerative enteritis result (a) After ileo-ileostomy? (b) After ileocolostomy? (c) When a simple blind loop of ileum is left distal to the anastomosis?

Accordingly, an obstruction was created in the ileum five to six inches proximal to the ileocecal valve in five dogs, by severing the bowel transversely and inverting both ends. The closed ends were approximated by suture in order to maintain the general relations of the ileum. In three a lateral anastomosis was made between the ileum twelve to fifteen inches proximal to the obstruction and the colon five to eight inches distal to the ileocecal valve (ileocolostomy). In two an ileo-ileostomy was established around the obstruction from points six inches and fifteen inches respectively proximal

* Vaughan: Transactions of the American Surgical Association, vol. xlviii, p. 266.

† Detailed experimental work to be reported elsewhere. Subject matter for a thesis as part of the requirement of the Graduate School of Medicine of the University of Pennsylvania for the degree of Master of Medical Science in Surgery.

to the obstruction. In two other dogs the ileum was severed, its ends turned in and an ileo-ileostomy made, permitting a blind loop of ileum to extend respectively six inches and eight inches beyond the anastomosis.

The post-operative course in the seven dogs was practically identical. They were fed a liquid diet for four days, a soft diet for three to four weeks and thereafter a general diet, including bones. For two to five weeks they remained well and active. A mild diarrhoea then developed and the dogs began to lose weight, became listless, and the diarrhoea progressively worse. Borborygmus and distension were noted. Two died of a perforated ulcer in the obstructed loop six weeks after operation, and the remainder were sacrificed.

Nine to fourteen weeks' post-operative autopsies showed practically identical findings in all these dogs whether ileo-ileostomy or ileocolostomy had been done or a blind loop of ileum left. The anastomoses were well healed and free from infection. The side-tracked and obstructed loop of ileum had elongated 50 per cent. and was dilated three to four times its normal diameter and its lymph-glands were enlarged. Numerous ulcers of various sizes were scattered throughout the loop and occasionally in the ileum proximal and the colon distal to the anastomosis. The dogs that died spontaneously died from a perforation of one of these ulcers. Furthermore, an advanced and widespread parenchymatous degeneration in liver and kidney occurred in all animals and it may be assumed that this occurs in clinical cases and would explain the great debility and slow convalescence frequently encountered.

Experimentally, then, an *ulcerative enterocolitis affecting chiefly the obstructed loop was produced in every way similar to the ulcerative enteritis of the clinical cases* by an obstruction in the ileum and a side-tracking anastomosis around the obstruction whether said anastomosis was ileo-ileostomy or an ileocolostomy. A similar condition was produced if a blind loop was left beyond or distal to the anastomosis.

It would seem, therefore, that with an entero-anastomosis for the relief of intestinal obstruction due to a mass of small intestinal adhesions if the obstruction recurs or persists an ulcerative enteritis and dilatation of the obstructed loop will occur, as the obstructed loop acts like a blind end left beyond a lateral anastomosis. If the obstruction is relieved and does not recur, the patient remains well.

Conclusion.—(1) Following an entero-anastomosis around a mass of intestinal adhesions, uneventful recovery is to be anticipated unless intestinal obstruction in the adherent coils persists or recurs.

(2) If the obstruction persists or recurs there will follow an ulcerative enteritis and dilatation of the obstructed loops leading perhaps to a general enterocolitis evidenced by diarrhoea, visible peristalsis, and borborygmus. Resection of the side-tracked ulcerated intestine will be necessary.

(3) Entero-anastomosis for intestinal obstruction must be looked upon as a possible first-stage operation of which resection of the obstructed loops may be required as a second stage.

OBSTRUCTED LOOP IN INTESTINAL OBSTRUCTION

(4) No matter whether the anastomosis be an ileo-ileostomy or an ileocolostomy, in the presence of obstruction the ulceration will occur.

(5) That the obstruction and subsequent stagnation play the major part in the cause of the ulceration seems proven by the fact that clinically and experimentally in a blind loop of intestine left distal to an anastomosis a similar ulceration will be produced; in other words, if the obstruction in the side-tracked intestine remains it acts like a blind loop left distal to a lateral anastomosis.

(6) In the presence of *acute* obstruction it would be unwise to consider primary resection of the obstructing coils unless gangrenous, but if at the time of lateral anastomosis it is *certain* that the obstruction in the adherent area remains, the two-stage operation must be definitely planned.

MAGGOTS AND OSTEOMYELITIS

BY WALTON MARTIN, M.D., AND WILLIAM G. HEEKS, M.D.
OF NEW YORK, N.Y.

AMONG the distinguished contributors to the fifth volume of the proceedings of the Inter-State Post-Graduate Medical Association appears the name of the late Dr. William Stevenson Baer, Clinical Professor of Orthopædic Surgery, Johns Hopkins University. In the report of his clinical address, are two pages on "Viable Antiseptics in Chronic Osteomyelitis."¹ The meeting was held in Detroit in October, 1929. In the meeting, as Doctor Baer was about to throw films on the screen to illustrate his treatment of osteomyelitis by maggots, he said: "I hope the editor of the American Medical Journal is here. I see in the August number there is a little squib put down on this subject under 'Fakes and Nostrums.'" I have been unable to find this reference, but if Doctor Baer were alive today, he could make no such comment. In the Journal of the American Medical Association of January 30, 1932, appeared among "New and Non-official Remedies," accepted by the Council on Pharmacy and Chemistry, "Surgical Maggots, Lederle."² In the March 12 issue, there is a two-page advertisement by the Lederle Laboratories on "The Development of Surgical Maggots," in which appears the statement that "The acceptance of Surgical Maggots, Lederle, by the Council on Pharmacy and Chemistry attests the approval of the maggot treatment by leading orthopædic surgeons. Its effectiveness has been so outstanding in chronic osteomyelitis that the treatment has been applied to other types of suppurating and sloughing wounds. Several clinics are using maggots in their out-patient departments on ambulatory cases of chronic leg ulcers and even carbuncles. Tuberculous abscesses and tuberculous bone lesions appear to respond with gratifying results." In the April 2 issue of the Journal of the American Medical Association there are two pages on the subject. Even at the meeting in Detroit, Doctor Baer's work received the endorsement of Dean Lewis, Professor of Surgery at Johns Hopkins University, who spoke at the end of a paper on acute osteomyelitis of Doctor Baer's results in chronic osteomyelitis as astonishing. He writes that "The grubs introduced by him in these bone cavities have separated the living from the dead bone without injuring the living bone."³

The interest in the method has not been confined to the medical profession. It has been considered to be of sufficient interest to appear in journals written to spread abroad scientific knowledge. In the *Science News Letter* (a weekly summary of current science), of August 22, 1931, there is an article by Jane Stafford on "How Clean Larvæ of the Blow Fly Are Carefully Bred to Destroy Germs Rather than Spread Them." I cannot do better in showing how so-called advances in science are reported than to quote extensively from this article. "The feeling about maggot treatment is not much different from the feeling your eighteenth-century ancestors had about small-pox vaccination . . . all

MAGGOTS AND OSTEOMYELITIS

sorts of arguments had to be refuted. Some people did not think it would give protection. Others thought it was too dangerous. . . . The use of maggots, tiny crawling larvae of the blow flies, to fight infection in wounds and to clear up the bone disease, osteomyelitis, was developed from observations made during the World War by an American surgeon, Dr. William S. Baer, of Baltimore. . . . The maggot treatment will probably not meet with as much opposition among physicians as did Jenner's vaccination method, because of Doctor Baer's high standing in the medical profession and the esteem with which physicians both in Baltimore and elsewhere regarded him."⁴

The following is taken from a recent newspaper regarding the maggot treatment as presented at the meeting of the American Medical Association in New Orleans: "Tiny pinhead maggots are proving expert surgeons in the treatment of bone infections, according to scientific exhibits of the American Medical Association meeting here today. The maggot surgeons were called into cases of bone infection where it was found impossible to remove all the infected bone with a knife. The maggots were sterilized before being put to work."⁵

As these statements, either based on or suggested by the observations recorded by Doctor Baer, are at variance with common knowledge, readily accessible in standard text-books on entomology, pathology and surgery, it has seemed to me worth while reviewing the subject carefully. I shall first refer to the statements regarding the anatomy and physiology of the maggot, then to those regarding the course of osteomyelitis and finally to those referring to the healing of an open contaminated wound.

In the Detroit meeting and as I heard Doctor Baer talk, in presenting his patients in his clinic in Baltimore in 1929, the efficacy of the treatment is based on the notion that the maggot gnaws away dead bone from living bone and shows a special activity in destroying bacteria. "The maggot goes directly to the bone itself. He likes bones as dogs do, rather than meat. He goes and gets at the bone and separates any sequestrum from the living bone, and not until he gets down to the bone itself, where it bleeds, will he stop gnawing the dead bone."

In the paper arranged for publication after Doctor Baer's death by Dr. George E. Bennett on "The Treatment of Chronic Osteomyelitis with Maggots,"⁶ these statements are modified; the maggots are said to suck up bacteria and consume dead tissue, bacteria pass through the intestinal tract and some bacteria are killed. The maggot is said to "work around and separate small sequestra and dead particles of bone still attached to normal bone and *seem* to gnaw down to the bone until bleeding bone is reached." But farther on, in the same paper, it is written that "the maggot has an intuition as to where the line of demarkation is going to appear and eats down to that line and thus removes all potential sequestra."

The bacteria are said to begin to diminish with the first hours of application and the original paper is headed "Viable Antiseptics."

These statements are not in agreement with those recorded by competent scientific observers and set down in standard text-books of entomology. There has been no disagreement about the fact that the maggots are capable of taking only liquid nourishment, since the original observation of Fabre made over forty years ago. Their mouth parts are so arranged that anything

like gnawing is impossible. There has been no disagreement regarding the hooklets near the cephalic end being organs of locomotion. There has been no disagreement about the maggots of blow flies living in nature with myriads of the bacteria of decomposition furthering, rather than inhibiting, their action. Common observation has made this familiar to all who have watched the decomposition of the cadaver of any small animal. The stench of putrefaction and the buzzing of blue-bottle flies are too frequently associated to escape notice. For many years, the maggots were supposed to be generated by corruption. "Maggotes ben wormes that brede of corrupt and rotyd moysture in flesshe" (1398). It is a common observation to see bones, hair and hide left after the flesh has melted away under the combined action of bacteria and larvæ. When there is no odor of putrefaction, the flies no longer visit the carrion.

But there has been much discussion as to the external digestion of the maggot and to the share played by bacteria in preparing suitable liquid food. It can no longer be doubted that ferments, to some extent, pass out of the body of the maggot into the medium in which it is living, and recent work has confirmed the observations and experiments of Woolman, that eggs can be hatched and maggots reared without bacteria, although growth under these conditions does not seem to be entirely normal.

It is of interest to review the work that led to these conclusions.

FABRE⁷ forty years or more ago, in one of his delightful studies on the habits and behavior of insects, brought out that the mouth parts of the maggots of the flesh flies are only adapted to sucking up nourishment in liquid form; that the two hook-like processes near the head are organs of locomotion. He placed larvæ in test tubes with fragments of protein material and showed how the material first became fluid, then was absorbed. He concluded that some subtle pepsin-like ferment was secreted externally which acted on the protein material and reduced it to a broth readily sucked up by the maggot. In another article, he demonstrated, by careful observation, a fact known for years, that cadavers in which the flesh flies lay their eggs and larvæ develop, liquefy much faster than those abandoned to the action of the bacteria of putrefaction alone.

In 1907, GUYÉNOT⁸ published a paper on the digestive apparatus and the digestion of the larvæ of the flesh flies, in which he attempted to disprove the conclusions of Fabre regarding the external digestion by a pepsin-like ferment. Guyénot's conclusions are accepted and set forth by L. O. Howard,⁹ principal entomologist of the United States Department of Agriculture, in a book on the fly (copyrighted 1911) and by A. D. Imms, professor of entomology in British India, in the "General Text-book of Entomology." IMMS (second edition, 1930)¹⁰ gives the following summary of the views of these two observers: "External digestion has been observed in divers orders of insects; in some cases it is of a preliminary nature only, while in others, the essential processes of digestion appear to take place outside the body. Fabre states that the larvæ of *Lucilis Cæsar* (one of the flesh flies) discharges the digestive secretion over the carrion that serves as its food. By means of a ferment analogous to pepsin, the protein matter is liquefied and subsequently imbibed. This explanation is disputed by Guyénot (1907) who states that the digestive secretion exhibits no such properties and that the functions ascribed to it by Fabre are in reality performed by symbiotic micrococci which are abundant in the food reservoir of the maggot."

It may be of interest to give in detail Guyénot's conclusions. He writes: "The diges-

MAGGOTS AND OSTEOMYELITIS

tion of the larvæ of flies results from a special mechanism, if it be true that the chemical elaboration of the food takes place outside, instead of inside, the digestive tube."

The hypothesis of this external digestion rested on the observation that the larvæ require nourishment in liquid form, and this conclusion is drawn from the following:

(1) He never saw larvæ in the presence of solid or pap-like food absorb the least particle of it before it had been made liquid.

(2) Repeated examination of the digestive tract of the larvæ (crop and intestines) showed that the contents were always liquid, and contained minute solid bodies visible only under the microscope.

(3) The larvæ have no apparatus of mastication, the cephalic hooklets serving only for the purpose of fixation and locomotion, being so arranged that anything like mastication is impossible. Not a particle is absorbed if maggots are placed in contact with finely divided carbon: if water is added to make a paste, only microscopical particles are taken in with the fluid.

Guyénot gives drawings of the mouth, the pharynx, the cephalo-pharyngeal skeleton with the hooklets, the crop and the intestinal tract of the maggot.

WOOLMAN¹¹ in 1922, in the *Annals of the Institut Pasteur*, in an article on the nutrition of the larvæ of flies, again reviewed the subject. After referring to observations of Guyénot, who had drawn the conclusion, as we have already pointed out, that the maggot secretes no soluble ferment, but lives on albuminous material liquefied by bacteria of decomposition, Woolman writes that "Nothing is easier than to confirm the digestive action, to some extent, of divers ferments outside the larvae, of which Fabre speaks. It suffices to take aseptic larvæ and place them on gelatine to see it rapidly liquefy. A glycerine extract of the pap upon which the maggots have fed shows the presence of protease." "It goes without saying," he writes, "that in nature, the action of proteolytic bacteria is added to the action of the digestive ferments of the maggot, but when the larvæ are placed in suitable conditions, development is perfect without bacteria."

In April, 1931, R. P. HOPSON, in the *Journal of Experimental Biology*,¹² in an article on the nutrition of the blow-fly larvæ, made a most painstaking study of the gastro-intestinal tract of the maggot and the ferments secreted. The crop appears to function as a storage organ only. The paper gives an account of the histology of the mid-gut and the physiology of digestion. The mid-gut of the larvæ of the variety of flesh flies investigated can be divided into three distinct regions, termed anterior, middle and posterior. Trypsin, peptidase and lipase are present in the mid-gut, the enzymes being concentrated in the anterior and posterior segments. The proteolytic enzymes persist in the excreta, therefore external digestion to some extent can occur without the aid of microorganisms.

No evidence has been presented by a competent observer that any ferment with solvent action on bone exists.

To estimate the results of treatment, it is well to study the individual case reports and to review the natural course of the disease:

"In some cases which had chronic osteomyelitis," Doctor Baer reported, "from two to ten years, and had been operated on two to fifteen times . . . we cut down on that wound (I assume by 'that wound' Doctor Baer referred to the sinus tract leading down to necrotic bone) and took out whatever sequestra we could find in the wound itself; then, after twenty-four hours, introduced as many maggots as the wound would hold, every fourth day introducing new maggots and washing out the old ones until at the end of that time all those wounds were healed. We had some twenty-one cases, both of compound fracture and ordinary chronic osteomyelitis of most of the bones of the human body and we have yet to have any one of those twenty-one cases fail to heal." (1929.)

In Doctor Baer's second paper details of treatment and results are given. As compound fractures and tuberculosis of bone joints present a problem somewhat different, I shall first refer to the case of hematogenous staphylococcus osteomyelitis, and as in young

children the cure is effected more readily than in older children and adults where the infection has persisted for a considerable period of time, I have selected all the case reports of staphylococcus osteomyelitis in patients of fourteen years or older.

In the table of case reports, there are twenty-eight such cases of staphylococcus osteomyelitis. We find only six reported as healed: case Nos. 8, 30, 38, 57, 73 and 82 (21.4 per cent.). Three are reported as "practically healed," Nos. 42, 62 and 63. In Case 42, the operation was performed December 3, 1930, the maggots inserted twenty times. On May 18, five months later, it was reported as "practically healed." I assume that this term is applied when a small dry crust or superficial sinus with a very small amount of discharge is left, which in the opinion of the surgeon is about to heal. Case 62, two months after the operation, was reported "practically healed." Case 63 was operated on June 13, 1930; the maggots were inserted twelve times; two and a half months later it was reported "practically healed," although in the report published six months later, no follow-up is reported.

Case Nos. 80 and 87 are reported as almost healed; in No. 80, the maggots were inserted five times. The operation was performed September 11, 1929, and on November 23, 1929, it was reported as almost healed. In case No. 87 the operation was performed June 26, 1930; the maggots were inserted seven times and six months later reported as almost healed.

Case Nos. 15, 59, 61, 65, 68, 70, 72, 74, 76, 84, 85, 88 and 89 are reported as improved; No. 15 is reported as much improved.

Case Nos. 66, 67 and 69 are reported as unimproved. In No. 66 the operation was performed July 10, 1930; the maggots were introduced eighteen times. The patient was sixty-eight years old, had had the lesion for ten years and had had four previous operations. Case No. 57, osteomyelitis of the right second finger, thirty-three years old, was operated on March 28, 1930; three times the maggots were introduced. On April 10, 1930, he was reported as unimproved. Case No. 69: There was osteomyelitis of the right femur and right ulna. Operations were performed on May 13, August 21 and October 28, 1930. The maggots were introduced twenty-eight times.

It is notoriously difficult to study the efficacy of treatment by controls such as used in all experimental work. True controls of clinical material in infection are nearly impossible on account of the variation in dosage and the virulence of the microorganism and the susceptibility of the host. But curiously enough, rough controls, so to speak, are furnished by studying the reports of Kalowski¹³ on the "Orr Treatment of Osteomyelitis" in the same volume of *Bone and Joint Surgery* as Doctor Baer's last report appears.

After an operation in which, through adequate incision of the soft parts, all sequestra were removed, overhanging bone edges made shelving, and the whole wound, packed loosely, wide open, with vaseline gauze, the joints above and below the diseased bone were immobilized. The forming granulations were left undisturbed by allowing the gauze packing to remain in place. One hundred thirty cases are recorded, ninety-nine are recorded healed, twenty-two unhealed, six amputations and three deaths. The number of healed is 76.15 per cent.

Unfortunately, details of the individual cases are not given; compound fractures and tuberculous osteomyelitis are included; no distinction is made regarding phases of infection; percentages are drawn from widely dissimilar types of infection. However, grouping all the cases together in similar fashion from Doctor Baer's records shows thirty-eight healed in eighty-nine cases (43.8 per cent.), or, including as healed the four reported as "practically healed," 47 per cent.

Further, to form a just appraisal of any method of treatment, it is necessary to review and consider the natural course of osteomyelitis.

It may be well to review first the experimental work which has contributed to an exact understanding of the course of hematogenous infection in bone. Over forty years ago, the course of infection was clearly demonstrated by a number of carefully carried out experiments. Lannelongue and Archard,¹⁴ in France (1890), Colzi¹⁵ in Italy in 1889 and later, Lexer¹⁶ in Germany (1897)—all produced by numerous experiments not only the general features but many of the details of the disease as it is presented in man.

Further, a second group of experimenters in attempting to elucidate the fate of microorganisms injected into the blood current, although not directly concerned with the lesions of osteomyelitis, recorded a number of careful observations on the distribution of microorganisms and minute inert foreign particles of the size of staphylococci in the bone-marrow, as well as the spleen, liver and other tissues of the body (Wyssokowitsch,¹⁷ Hoba,¹⁸ etc.).

These experiments and observations make it clear that staphylococci and minute particles of inert lamp black introduced into the ear veins of rabbits, for example, rapidly disappear from the circulating blood. If the animals are killed, the particles are found scattered throughout the body, but especially in the liver, spleen and bone-marrow, settling out where the circulation in the wide capillary area is unusually slow. There they come in contact with special cells which have the property of taking up minute foreign particles and destroying living microorganisms. If the mass action of introduced organisms is sufficient, or the local resistance is lowered by a variety of external conditions, instead of being destroyed, they start to grow, pouring countless millions into the blood-stream.

The conditions in the growing bone of young animals is peculiar. The capillary mesh work is so formed that particles of carbon introduced settle out in such masses in the capillaries of the marrow in the portion of the shaft of the long bones near the epiphyseal cartilages, that the structure can no longer be made out.

In all generalized infection, the capillary mesh work of the bone-marrow is concerned in the destruction of countless microorganisms. If there is local lowering of resistance, the lodged microbes may make their presence known by local lesions in one of the bones and the contiguous joints, thus streptococcus osteomyelitis, pneumococcus osteomyelitis, typhoid osteomyelitis, tuberculous osteomyelitis, syphilitic osteomyelitis, even glanders osteomyelitis, etc., are recognized, as well as similar forms of arthritis. Each has certain characteristic features and predilection in localization.

But all forms imply that the infecting agent has been deposited in the capillaries of the bone-marrow during the generalization of infection; each shows a great variety in the lesions produced. The reaction may be so slight that it escapes clinical observation, or the reaction may lead to extensive local lesions accompanied by exudate and mass necrosis.

The acute hematogenous osteomyelitis of childhood, as it is understood clinically, is due usually to staphylococcus (75 per cent.); occasionally to streptococcus.

LANNELONGUE¹⁹ was able to make the following distinctions between these two forms experimentally. The animals used were young rabbits, weighing between 500 to 1,300 grams. The inoculations were made in the veins of the ear. The quantity injected varied between 0.25 and one cubic centimetre of bouillon culture. The amount necessary to create the lesion was a little larger for the streptococci than for the staphylococci. The histological examination of the bone showed lesions in every way similar; there were masses of microorganisms in the medullary substance and in the Haversian canals. There were also accumulations of microbes in the capillaries in the neighborhood of the epiphyseal cartilages. The morbid localization in the skeleton showed itself under three forms; sub-periosteal abscesses, abscess and purulent intermedullary infiltration and articular suppuration. The intra-osseous foci was situated five times in the inferior portion of the femur, three times in the inferior portion of the tibia, once in the inferior extremity of the humerus and once in the superior portion of the ulna. Suppurative arthritis was observed in both forms, but far more frequently in the streptococcus inoculation. A detail of interest was that in the suppurative arthritis in both forms, the articular cartilage presented no appreciable alteration, even after it had been exposed to the purulent exudate, except that there were particles of fibrin adherent to the joint surface and infiltrated with microbes; the articular cartilage was intact, its fundamental substance was not altered, in contrast to the diaphyseal cartilage which was frequently invaded and destroyed. The bone lesions were accompanied by necrosis far more frequently in staphylococcus infection.

Acute osteomyelitis of infants and young children represents the osteo-arthritic localization of a generalized pyogenic infection.

It has been my good fortune to have associated with me on my service at St. Luke's Hospital, for the past twenty years, the attending surgeon to the Babies Hospital. Knowing my interest in generalized infection and its relation to osteomyelitis, Dr. W. A. Downes, the late Doctor Bolling and at present Doctor Donovan have been kind enough to allow me to see in consultation from time to time infants and young children with general staphylococcus and streptococcus infection, especially those with osteo-arthritic localization, and have given me the opportunity to study and follow residual bone lesions. I have appended to this paper a group of case reports prepared by Doctor Heeks, assistant surgeon to my division at St. Luke's Hospital, and assistant surgeon to the Babies Hospital. The study of the sequence in the pathological lesions in the patients that have recovered is most interesting and the autopsy findings are of equal interest. They are startlingly similar to the findings in experimental inoculations reported by Lannelongue. These infants and young children are of especial interest in so far as they probably represent infection in non-sensitized or imperfectly sensitized subjects. I believe the acute osteomyelitis of adolescence and the uncommon acute osteomyelitis of adults is best explained as an autogenous or exogenous reinfection in sensitized subjects, with high general resistance and marked tendency to local destructive lesions; the autogenous infection resulting from the awakening of hibernating microorganisms from an undetected latent foci in the medullary cavity; the exogenous infection from the settling out in the bone-marrow of microorganisms from primary lesions in skin or mucous membrane similar to the primary lesions which precede acute staphylococcus infec-

MAGGOTS AND OSTEOMYELITIS

tion in infancy and early childhood, such as furuncles, pustules, infected cracks and fissures, small infected wounds, etc.

It is well recognized that a staphylococcic lesion of the dense derma, such as is seen in a furuncle and representing focal infection in a sensitized subject, usually terminates, if left to itself in a local area of necrosis, and that the necrotic area is surrounded by an area of infiltrated, swollen, reacting tissue; and that when the necrotic core comes away as a purulent blob, the whole process rapidly subsides; further, that a focal staphylococcal infection which has led to a purulent exudate, surrounded by a wall of reacting tissue, rapidly subsides when free exit is given to the purulent exudate.

Similar lesions occur when staphylococci are implanted in bone, but they are modified by the impregnation of the ground substance of the connective tissue with the salts of lime, making a framework which dissolves and disintegrates with difficulty, and by the process taking place in such a way that the reacting new-formed bone tissue usually locks in, to a greater or less extent, the necrotic tissue.

Chronic staphylococcus osteomyelitis is in most instances but the expression of these simple considerations. Chronic osteomyelitis may be said to represent a residual or tertiary lesion in generalized staphylococcic infection, modified by the peculiarly resistant bone tissue, with its two characteristic groups of cells—one group concerned with the laying down of new bone in the reacting area, the other group concerned with the eating away of bone resulting in the separation and absorption of dead bone. It represents a terminal stage of infection with a marked natural tendency toward recovery.

The failure to cause sound healing in chronic pyogenic osteomyelitis is due to the imprisonment of necrotic bone or small foci of infection, by the surrounded new-formed bone, and by the rigid walls of bone cavities formed about such foci as infection. The sequestrum, that is to say, the detached necrotic bone has the same significance in the tissues as any infected foreign body has. From time to time the tissue may heal about it, if the foreign body is very small and the infection much attenuated, but sooner or later, due to local lowering of resistance, the latent infection becomes active, exudate collects under pressure and escapes externally. With each reinfection the surrounding tissue becomes thicker and the thickness and rigidity of the walls bears not only relation to the duration of the infection but to the amount of tension or pressure set up by the exudate, when it is intermittently dammed back or imperfectly drained.

This is true for chronic infection in bone as it is true for the thickened pleura in chronic empyæma.

If left untreated, if the exudate is allowed time after time to collect under pressure, with intermittent discharge, if it is repeatedly reinfected with new microorganisms from without, the reacting new formed bone gradually becomes thicker and denser. Enormous thickening may occur in the new bone about the sequestrum, which is but a porous insoluble foreign body, saturated by decomposing wound discharges and swarming with bacteria.

If the sequestrum is minute and the infection attenuated, intermittent low-grade infection may result, making the various forms of condensing and hypertrophic osteitis.

Chronic abscesses, shut in by eburnated bone, rigid walled bone cavities, hyperosteoses, local or extending over the entire shaft, various forms of condensing osteitis, imprisoned and free sequestra and attached necrotic bone and bone fistulæ connected with any of these forms, through which, for months and years, continuous or intermittent purulent discharge takes place, and low-grade secondary infection in the reacting bone formed by dammed back exudate make up the clinical picture of chronic osteomyelitis. A most satisfactory description of the various forms of chronic osteomyelitis was given by Lannelongue fifty-three years ago. It is based on eighty observations.

Any operation that sets right the morbid anatomical condition in this terminal stage results in permanent cure, but the difficulty of the operation bears a direct relation to the duration of the disorder and the preceding management of the case and the anatomical situation of diseased bone.

In the terminal stage, the essentials of treatment are the removal of sequestra and the obliteration of rigid walled cavities. The treatment is based on wide incision of the soft parts, affording complete access to the diseased area. It is planned by a knowledge of the most advantageous anatomical approach to the diseased bone rather than by the position of the sinus. The new-formed bone is cut away freely over the focus of infection and no attempt made to remove a sequestrum until it is exposed throughout its whole length. Breaking sequestra and leaving behind fragments is a disaster. The attempt is made to cut away the bone in such a way that the resulting gutter or trough has shelving sides.

There is a general agreement on these principles. It is advised by Baer as a preliminary to the introduction of maggots. There is a distinct advantage in waiting until the X-ray shows the dead bone detached from the living. If the attempt is made to remove the necrosed bone before it is detached (I am speaking of staphylococcus osteomyelitis) much sound bone may be sacrificed. It is astonishing to compare X-ray pictures of reacting bone during the earlier stages of infection with the same bone some months later. The irregular deposit of lime salts in the newly formed bone, shown by lessened density and irregular mottling of the shadows, and the alteration of contour suggest a widespread lesion, but the same bone two or three months later may show a nearly normal contour and a small sequestrum readily removed by a simple operation. The most distressing cases that have come to my attention have been those in which ill-advised attempts have been made to remove most of the reacting new-formed bone under the impression that it was necrotic bone.

In circumscribed abscess in bone, it suffices to cut away the bone over the abscess, making sure that the opening in the bone is as large, if not larger than the cavity itself.

The rigid walled cavity left in bone after any of these operations requires

treatment according to the size of the cavity, its position in the bone and the virulence of the infection. Small cavities with attenuated infection heal rapidly and soundly, and remain healed after an exit is made for the exudate.

Larger cavities are best treated by some effort to obliterate the walls and allow the soft parts to fall in. Large cavities near the joints usually made by the surgeon scraping away healing bone are extremely difficult to close. Experience gained in a somewhat different field (I refer to infected gunshot wounds) shows satisfactory closure by pedicle flaps turned into the cavities, first prepared by reducing the surface infection. I have reported elsewhere the results of the treatment of bone cavities.²⁰

My experience, derived from 200 or more patients that have come under my observation of all varieties of hematogenous osteomyelitis, has led to the belief that the majority heal rapidly and permanently under suitable treatment. I have watched some of these patients for fifteen and twenty years. I have seen them grow to manhood, engage in sports where the originally diseased area is subjected to repeated trauma. The recurrences I have had have resulted from obvious failures on my own part in carrying out the simple principles involved. I have broken and left behind fragments of sequestra; I have had superficial necrosis of skin and recurrent superficial infection of underlying bone in areas where the skin has become adherent to the bone, from badly planned scars. I have delayed so long to remove a sequestrum that the density of bone made it very difficult to detect and remove a small focus of infection causing recurring infection.

I have frequently been unwilling to advise operation in adults with slight persistent lesions without disturbance of general health and with trifling disability where the operation required would demand wide exposure and prolonged incapacity. I have at times been hindered from making suitable exposure by timidity. Fear of spreading infection where the pelvic bones were involved or the occipital bone near the foramen magnum, for example, has made me temporize rather than attempt a radical operation. I have seen many so-called recurrences due to infection in other bones, or portions of the shaft beyond the original focus. I have seen several instances of the sudden awakening of infection at the site of the original lesion, years after the original lesion, in one instance thirty-six years.²⁰

Purulent collection beneath the periosteum or in the substance of bone in acutely ill children with general staphylococcus septicemia is treated most advantageously by giving exit to the purulent exudate at the earliest possible moment and by the simplest means. During the stage when the acute stage is subsiding, during the establishment of residual lesions, every effort is made to detect and drain local collections of pus, not only at the site originally, but in other bones, soft parts, *etc.*

In most instances, one or more operations are necessary before attempting to treat the residual lesions and such residual lesions often heal under the simplest treatment. The removal of a detached sequestrum results, usually, in a rapid and permanent cure.

Therefore, the number of operations does not carry with it, necessarily, the implication of inadequate treatment. So-called radical operations on an infected bone in a young child suffering from generalized staphylococcus or streptococcus infection with the idea in mind of avoiding all subsequent operations is thought ill-advised by all who have had experience with this phase of osteomyelitis. Dean Lewis, in his paper on acute osteomyelitis, already referred to, emphasized this point by recalling the interesting experience of Wilms and Enderlen at the Heidelberg Clinic.

The cure of chronic osteomyelitis cannot be considered extraordinary if it consists of the early removal of a free and readily accessible sequestrum; many such patients heal with astonishing rapidity. A few heal by spontaneous emergence of the sequestrum without operation.

A careful statistical study of osteomyelitis made forty years ago by Haaga²² from 407 patients treated at the Bruns Clinic is interesting. The localizing in the long bones, the frequency of multiple localizations and the outcome are all tabulated. These records agree in general with observations made by all those who have considered the subject. The number of multiple lesions was considerable. There were 559 bony lesions observed in the 407 patients; of the 559 lesions only forty-nine healed without necrosis; of the 490 in which necrosis occurred, only forty-seven healed by spontaneous emergence of the sequestrum. The different bones behaved differently in this respect; ten times in fifty-five cases a sequestrum of the humerus discharged of itself, but this occurred only five times in the femur in 157 cases and only thirteen times in the tibia in 225 cases. In forty-seven, operations were not performed for various reasons. Four hundred and twelve of the 490 patients are reported as healed after the operation (84 per cent.).

To judge results in chronic osteomyelitis is difficult. It is well to remember, before drawing conclusions of any method of treatment, that hematogenous osteomyelitis is but one of the localizations in bone of a generalized infection, and that necrosis is not a disease; it is but the termination of a great number of infectious lesions of bone.

I find it confusing to include among cases of hematogenous pyogenic osteomyelitis, tuberculosis of bones and joints, and compound fractures, just as I should find it confusing to include syphilitic osteomyelitis. Each of these types of infection presents special features and demands separate consideration.

Tuberculosis of bones and joints represents localization with destructive lesions and marked general resistance. They are metastatic or tertiary lesions. Not infrequently, these focal lesions heal under simple measures: By exposure to sunlight, immobilization alone, various operations producing ankylosis of joints with incomplete excisions of the tuberculous focus, and so-called complete excision of the focus are followed by cure. All who have had considerable experience with this group of lesions agree in making every effort to avoid secondary pyogenic infection. This is as true after operations on the bones and joints as after the removal of a tuberculous kidney or uterine tube, or after operations for tuberculous peritoneum or after the

MAGGOTS AND OSTEOMYELITIS

excision of a tuberculous gland. The body cells seem to take care of the residual tuberculosis inevitably left, even after the most painstaking operation, far better if the tissues are not superficially infected with pyogenic organisms.

Doctor Baer's list includes six reports of tuberculous lesions, Nos. 3, 34, 36, 47, 75 and 83. There was one death from tetanus; two are reported unimproved; 50 per cent. are reported cured.

As we all know, in a compound fracture, there is a wound of the soft parts which communicates with the broken bone. Such a wound may not be soiled with the pathogenic bacteria, or the bacteria may be few in number, or the wound may be heavily contaminated. A compound fracture is by no means necessarily followed by traumatic osteomyelitis; many heal like a simple fracture without any established infection in the broken and damaged ends of the bones. Here again, every effort has been made for the last sixty years to avoid introducing new pathogenic bacteria after the injury.

Doctor Baer's report includes seven cases classified as compound fractures, Nos. 45, 48, 51, 54, 56, 78 and 81. All seem instances of traumatic osteomyelitis. In Case 48, however, the patient came under treatment four days after the injury; the infecting organism was reported as the staphylococcus, but there is no mention of whether cultures were taken from the bone or the wound in the skin. Four are reported healed, three improved. In Nos. 51 and 54, there is no record of the introduction of maggots.

The treatment of compound fractures by this method brings up a curious confusion in both of Doctor Baer's papers regarding secondary infection, the relation of antiseptics to infection and the reason for the use of antiseptics and of materials sterilized by heat as applied in modern technic, and the distinction between a contaminated wound and an infected wound.

Doctor Baer writes: "Nothing was used upon the skin of the patient except some slight scrubbing with normal salt solution, and no antiseptic whatever was brought in the neighborhood of the wound. The operation was done with bare hands, washed only in water, and while no gloves were used, no iodine or any other chemical preparation was applied to the wound itself before operation. The idea was that if the wounds healed up by means of the introduction of the maggot, the maggot alone would be responsible for the cure and no chemical agent could be said to have had anything to do with the result; and, if the wound healed, the maggot would not be injured or its activity decreased by bringing it in contact with any chemical substance."

The impression conveyed seems to be that the sterilization of the skin of the patient with an antiseptic and the wearing of gloves sterilized by heat might, in some way, invalidate the results of the maggot treatment. But it is generally recognized that these measures are not taken with any notion of the effect of chemicals on deep-seated, established infection. One would, in fact, by operating with bare hands not thoroughly cleansed, through unsterilized skin, be far more likely to confuse the issue of any given therapeutic measure through the danger of introducing in this way strains of virulent streptococci, tetanus bacilli, *etc.*, not in the original focus. He seemed to have believed that antiseptics were applied to destroy microorganisms long established and living in the walls of the reacting tissue. He seemed to have failed to distinguish between the use of antiseptics to limit or prevent the introduction of new virulent microorganisms from without, with the application of antiseptics to control established infection.

Early in the war, all efforts to disinfect the contaminated tract of missiles with chemicals were recognized as futile. It had been proved experimentally by Muller²³ and Koller²⁴ seventeen years before the war.

Nor were antiseptics such as Dakin's solution, for example, introduced with the idea of sterilizing the deeper tissue. They were introduced to wash away dead leucocytes, detritus, shreds of tissue, *etc.*, after a thorough surgical excision of the entire surface of the contaminated wound to the depth of two millimetres. It was well recognized and set down in the book on infected wounds by Carrel and Dehelly,²⁵ the exponents of the disinfection of wounds by neutral solution of sodium hypochlorite, that no matter how many times the bacteria were washed away, they would rapidly spread again over the entire wound surface as long as particles of necrotic tissue or infected foreign bodies remained. All who have studied the subject have reached the same conclusion. They were measures used to help the natural cleansing of an open, contaminated wound. Equally satisfactory results, however, were obtained by Douglas, Fleming and Colebrook²⁶ by flushing with 5 per cent. salt solution.

It has long been recognized and set down in text-books that no wound with established infection and no metastatic focus can be disinfected by a chemical solution. "The microorganisms are in the reacting tissue and beyond the reach of a chemical."²⁷

It may be well to recall that after a collection of pus has been evacuated or a sequestrum removed and after all the diverticulæ and communicating cavities have been opened, and a suitable exit made for wound discharge, a condition is created, favorable for the local defense reaction, but in most instances there are still innumerable microbes on fragments of attached necrotic tissue, in minute cracks and crevices in the infected surface. Moreover, there may be a delicate balance between the local defense reaction and the living microbes still in the zone of reacting tissue which can be readily turned one way or another.

The flow toward the surface of lymph and active living phagocytic cells, on which the destruction of bacteria in the walls of an infected cavity depends, the activity of cells which are concerned with separating the dead tissue from the living, the amount of destruction of leucocytes on the surface, with liberation of tryptic ferments so that the balance between the antitryptic and tryptic properties of the wound secretion are not disturbed, are all of great importance to maintain. Usually all is set right by the evacuation and maintenance of a free exit for wound discharges. To promote and hasten the cleansing of the infected wounds, after these essential conditions have been established, is the aim of the various ancillary measures.

The subject of infection of granulation or the infection of flowing discharges of an open contaminated wound was carefully studied during the first years of the war by Sir Almroth Wright.²⁸ He showed that the lymph-like discharge of an infected wound, when first poured out, contained mostly streptococci and active phagocytic cells, but that after it had collected in the

MAGGOTS AND OSTEOMYELITIS

wound it was an opaque exudate presenting the usual characteristics of pus. The chief bacterial agents at work were the streptococci, staphylococci and the *Bacillus proteus*.

The factor that comes into play in the change of the appearance of the exudate is the amount of tryptic ferment liberated by the disintegrating leucocytes. In other words, there is a trypsin-like ferment working in an alkaline medium in all open suppurating wounds.

The original observations of Doctor Baer on which he based his ideas were drawn from seeing two wounded soldiers recover who had been without aid for seven days. I will give the story in his own words. "Two soldiers with compound fractures of the femur and large flesh wounds of the abdomen and scrotum were brought into the hospital. These men had been wounded during an engagement and in such a part of the country, hidden by brush, that when the wounded of that battle were picked up they were overlooked. For seven days they lay on the battlefield, without water, without food and exposed to the weather and all insects which were about that region. Upon their arrival at the hospital I found that they had no fever and that there was no evidence of septicæmia or blood poisoning. Indeed, their condition was remarkably good, and if it had not been for their starvation and thirst, we would have said they were in excellent condition. . . . On removing the clothing from the wounded part, much was my surprise to see the wound filled with thousands and thousands of maggots, apparently those of the blow fly. The maggots simply swarmed and filled the entire wounded area. The sight was disgusting and measures were taken hurriedly to wash out these abominable looking creatures."

Unfortunately, no distinction is made, in the description, between the wounds of the two soldiers. They are described as if they were similar. There is no mention of the type of projectile; whether the injury was caused by fragments of shell casing, by a rifle bullet, by metallic splinters from an exploding hand grenade, shrapnel ball or secondary projectiles hurled into the tissue by bursting shells such as stones, splinters of wood, *etc.*, is not recorded. There is no description of the wound of entrance or the wound of exit. The injuries are simply referred to as compound fractures of the femur. The wounds were covered with maggots. When the maggots were washed away the granulations were pink, even and healthy-looking.

I think many who have had an opportunity to treat infected wounds in large out-patient departments have seen on rare occasions wounds infested with maggots. The few instances I have seen bear out exactly Doctor Baer's statements. I remember many years ago seeing a granulating wound of the external surface of the arm. When the filthy dressings were removed, saturated with decomposing wound discharges, the surface was found covered with maggots; the granulations were pink and healthy-looking. Several of the papers that have appeared during the last year have referred to records of the older surgeons telling of the good appearance of the granulations when the wound was infested with maggots.²⁹

The explanation that has seemed to me most reasonable is that the female flesh fly laid her eggs after a sufficient barrier of leucocytes and granulations had formed to prevent infection of the surface by the microorganisms on the feet and proboscis of the fly. It is well to keep in mind how rapidly this protecting wall forms in an open wound, so that bacteria falling into the wound after ten or twelve hours, if there is no interference with wound discharge, may live and multiply on the wound discharges and the detritus on the superficial granulations but do not penetrate the deeper tissues. The experiments of Giani³⁰ are interesting in this connection. He made open wounds in animals, very susceptible to anthrax. Filter paper soaked in virulent cultures of anthrax bacillus was laid on the open wounds, as gently as possible. All the animals died if the infected filter paper came in contact with the wound under six hours; after twelve hours, they all lived. Between six and twelve hours, half lived and half died. In those that died, slight hæmorrhage indicated that the protecting wall had been mechanically broken in placing the filter paper.

The adult flesh fly, like the house fly, is "more or less bristly and well capable of carrying microorganisms from putrescent or semi-liquid substance, but the mouth parts and feet are especially adapted to the purpose." Female flies must have deposited their eggs on the open wound surface in the soldiers referred to by Doctor Baer. They must have walked over the wounds palpating with their proboscis and feet, seeking a suitable place for the introduction of the ovipositor. The female flesh flies passed their pupal state, probably, in the superficial soil of the field of battle. They developed from maggots feeding on neighboring cadavers. The proboscis and feet and the bristly hair of the body of the female fly were probably soiled with the bacillus of Welch, the tetanus bacillus as well as innumerable bacteria of decomposition. I should draw the conclusion that the original wounds inflicted in these instances had not been heavily contaminated and the flies had crawled over the wound a sufficient time after injury to have avoided secondarily infecting the wound. I should assume that the maggots, by consuming the detritus and dead leucocytes, had indeed furthered the clearing of the wound, but that the two soldiers referred had escaped infection in spite of the flies. I do not believe that "the maggots had saved the lives of those two people and had acted as disinfecting agents."

Flies, hatched in excreta of man or animals (such as house flies), or in putrefying cadavers (such as flesh flies) and alighting on fresh wounds, have justly been considered the most dangerous of all the disseminators of pathogenic microorganisms. That these facts came finally to be recognized by Doctor Baer and his associates is made evident by their efforts to rear sterile maggots. It seems very improbable that the flies that laid their eggs or the maggots that hatched in wounds of soldiers left out on the field of battle were sterile.

In conclusion, it is safe to say that the maggot of the flesh fly is not a

MAGGOTS AND OSTEOMYELITIS

"Viable Antiseptic"; it multiplies and flourishes in some sort of symbiotic relation with the myriads of bacteria under natural conditions.

Its mouth parts are adapted only for taking fluid or pap-like nourishment. It cannot "gnaw bone like a dog," and no evidence has been presented that "the maggot has intuition as to where the line of demarkation is going to appear and eats down to that line and thus removes all potential sequestra."

In the conclusion in the last paper on the subject, the maggot treatment is not even spoken of as a treatment of osteomyelitis. It is said to be "a tremendously useful adjunct to thorough surgical treatment for chronic osteomyelitis, and, in our opinion, far more successful in securing permanent healing of these extensive wounds than any other method tried by us."

But no evidence is presented in the case records of the greater efficacy of this method of treatment. The records show far lower percentages of cures than are reported by the Orr treatment or than were reported forty years ago by Haaga.

The enthusiasm generated by the paradox that two severely wounded men, left untreated on the field of battle for seven days, recovered, seems, possibly, to have led to undue fervor in advancing an ancillary measure that might be used to promote the healing of a contaminated wound and that seems to have no essential relation to the cure of osteomyelitis.

ACUTE STAPHYLOCOCCUS AND STREPTOCOCCUS HEMATOGENOUS INFECTION WITH OSTEOARTHRITIC LOCALIZATION. STAPHYLOCOCCUS SEPSIS

S. M., aged four years, eleven months, admitted April 25, 1931; discharged August 12, 1931. Diagnosis.—Acute suppurative osteomyelitis of shaft of femur. Symptoms and Findings.—Traumatic injury to knee two weeks before, followed by cold and nasal discharge; had pain in left ankle for six days; pain in knee. Diagnosed by family doctor as rheumatic fever. Temperature for past two days— 104° . Physical Examination.—Slight swelling of knee; swelling and exquisite tenderness of lower femur. April 26, blood culture staphylococcus aureus hemolyticus. Wound culture staphylococcus aureus hemolyticus. X-ray Findings.—May 5, acute osteomyelitis of shaft of femur which at this time shows many destructive lesions. July 13, considerable involucrum formation; appear to be several sequestra. Operation.—Osteotomy of shaft of femur. Arthrotomy of knee-joint. Course.—Temperature on admission was 106° and ran a wavering course for forty days post-operative, then remained normal. Thirty-third post-operative day fell from chair and fractured lower third of femur. Skin traction applied. Discharged 108 days after operation in excellent condition with small draining sinus. Result.—Cured. Follow-up.—November 25, 1931, small sequestrum one inch long removed. December 9, 1931, wound well healed and walks well.

R. A., aged fifteen months, admitted August 9, 1930; discharged December 24, 1930. Diagnosis.—Hemolytic staphylococcus albus bacteremia with metastases, lobar pneumonia (group undetermined); dislocation both hips (everted dorsal); rickets; acute suppurative arthritis of hip-joints and shoulder. Symptoms and Findings.—Temperature for sixteen days; treated in outside hospital; five transfusions; but did not improve. Physical Examination.—Acutely ill septic child; infected transfusion wounds in both anti-cubital fossæ; sloughing wound in right groin; râles in both lungs; severe rickets. August 12, blood culture hemolytic staphylococcus albus. September 16, no growth in blood culture. November 26, blood culture—hemolytic staphylococcus albus (onset of pneumonia). Kahn, 0; tuberculin, 0. X-ray Findings.—August 10 bron-

chopneumonia; osteomyelitis of upper metaphyses of both humeri. January 23, 1931, review of films shows patient was originally case of severe rickets with multiple osteomyelitis. Seems probable that there were definite osteomyelitic changes present in proximal metaphysis of right tibia and both distal tibial metaphysis. At present bones show healing (complete) of rachitic lesions of left humerus at femoral heads and in distal tibiae. Lesion of right proximal tibia not completely healed. Bilateral dislocation of hips. Operation.—Transfusion 160 cubic centimetres whole blood. August 26, incision and drainage of wrist. September 5, arthrotomy of left shoulder. September 15, arthrotomy of hip-joints. September 25, arthrotomy of knee-joint. October 18, abscess of right leg incised. Course was prolonged. Developed multiple suppurative foci, all of which cultured hemolytic staphylococcus except left hip which cultured pneumococcus. Given autogenous vaccinal therapy. After fourteen weeks of septic temperature it became normal. Three weeks later developed a pneumonia in right upper and lower lobes; resolved. Result.—Cured. Subsequent History.—Wounds all well healed at time of discharge. No limitation of joint motion. Referred to Orthopedic Hospital for treatment of dislocated hips.

D. C., aged eight years and four months, admitted January 6, 1931; discharged April 1, 1931. Diagnosis.—Acute suppurative osteomyelitis of pubic bone; hemolytic staphylococcus albus. Symptoms and Findings.—December 25 fell and bruised right hip; two days later developed a boil on buttock; two days later developed pain in thigh and hip. Headache and fever with slight chill two days before admission. Physical examination showed pain on pressure and motion of head of femur (left muscle spasm). Temperature $103\frac{4}{10}^{\circ}$. X-ray Findings.—Reported negative until January 26 but review of films shows lesions sufficiently marked for diagnosis. January 6, lesion beginning in lower ramus of pubis close to synostosis of ischium. Course.—Temperature remained elevated until January 31. January 10, developed severe inguinal and femoral adenitis. (Tuberculin 1-1000 negative.) January 12, local tenderness over pubis; hip improved. January 16, hip-joint aspirated (after orthopedic opinion) clear fluid obtained. January 19, left-sided fullness on rectal examination. January 28, first reported X-ray evidence of osteomyelitis of pubis. January 31 operation. Fall of temperature to normal. Result.—Improved. Follow-up.—July 28, wound nearly healed; walks without difficulty. October 19, patient moved to Washington. No report can be obtained.

O. G., aged eleven years and five months, admitted June 2, 1931; discharged June 8, 1931. Diagnosis.—Anatomical diagnosis (autopsy):—acute periostitis of left tibia; cellulitis of lower leg; suppurative phlebitis of left saphenous vein; bacteremia staphylococcus aureus; (infarcts of lung); abscess of lungs, heart and kidneys; acute serofibrous pericarditis; acute fibrous pleurisy; bronchopneumonia. Symptoms and Findings.—Perfectly well until four days before admission then complained of pain in left thigh; no fever. Symptoms rapidly increased with headache, chills and fever. For past day, pain in left ankle with swelling and redness of leg. Temperature 105° on admission with diagnosis of acute rheumatic fever. June 6, culture of pus from wound showed hemolytic staphylococcus aureus. June 2, blood culture—staphylococcus albus. (contaminate?). June 7, blood culture—staphylococcus aureus. Operation.—June 6, incision and drainage of sub-periosteal collection of pus. June 6, transfusion 300 cubic centimetres whole blood. Course.—June 5, delirious, appears septic; leg swollen from foot to knee; red, hot and tender. No localization of abscess in leg. Pain in right elbow. June 6, patient became rapidly worse. Operation.—Collection of subperiosteal pus drained from lower third of left tibia. Result.—Died.

C. B., aged eleven years, admitted October 18, 1929; discharged October 10, 1930. Diagnosis.—Acute suppurative osteomyelitis of shaft of left tibia (staphylococcus albus hemolyticus); acute suppurative arthritis of left knee-joint. Symptoms and Findings.—Temperature, vomiting and headache for three weeks; pain and redness of both elbows for two weeks, then subsided; cervical spine and both hips became painful;

MAGGOTS AND OSTEOMYELITIS

small red spot over left tibia for three weeks, progressively becoming worse. Physical examination showed swelling of entire left leg; abscess over upper third of tibia; culture of pus from abscess and knee-joint contained hemolytic staphylococcus albus. No record of blood culture. X-ray Findings.—October 18 acute osteomyelitis of upper end of tibia. February 5, 1930, old osteomyelitis of tibia showing evidence of repair. July 8, 1931, no evidence of sequestrum. Operation.—October 18, incision and drainage of subperiosteal abscess of left tibia. November 16, arthrotomy of left knee-joint. May 8, 1930, incision and drainage of abscess of post-crural region. Course.—Cast applied to leg after arthrotomy; small sequestra removed at frequent intervals through sinus in leg. May 25, 1930, knee manipulated under anaesthesia to free adhesions. Allowed to walk with brace. July 10 lower sixth of femur fractured during manipulation of knee under anaesthesia. Result.—Improved. Subsequent History.—At time of discharge general condition was good. Had small sinus draining from tibia; walked well but had some stiffness of knee. Follow-up.—Referred for treatment to St. Luke's Hospital following discharge because of over age.

B. V., aged nine years and six months, admitted July 6, 1930; discharged October 10, 1930; readmitted December 25, 1930; discharged December 27, 1930. Diagnosis.—Acute suppurative osteomyelitis of upper third shaft of femur; acute suppurative arthritis of hip-joint; septicaemia; two abscesses. Symptoms and Findings.—Pain in right hip for five days; vomiting, fever and headache eight days; temperature 106° ; blood culture hemolytic staphylococcus albus, (at Hackensack Hospital). July 7, blood culture; no growth. X-ray Findings.—No changes apparent on admission; gradually appeared rarefied area involving trochanter and upper sixth of femur. December 16, no evidence of extension distally; evidence of articular and epiphyseal involvement. Operation.—July 19, 1930, arthrotomy of hip. Immobilized in plaster cast. Culture of pus showed staphylococcus albus. Course.—No complication. Discharged to convalescent hospital. All wounds healed. Result.—Improved. Subsequent History.—Superficial abscess of trochanteric region opened six months after first admission.

W. S., aged ten years, admitted August 3, 1930, discharged November 14, 1930; second admission February 17, 1931, discharged April 8, 1931; third admission June 30, 1931, discharged September 30, 1931; and fourth admission December 7, 1931, discharged December 11, 1931. Diagnosis.—Acute suppurative osteomyelitis of upper end of left tibia. Acute suppurative arthritis of right hip; chronic osteomyelitis of tibia; chronic osteomyelitis upper end of humerus; chronic osteomyelitis of humerus. Symptoms and Findings.—Painful left knee for eight days. Patient was struck blow in knee two weeks before; delirious past two days. Temperature 104° on admission. Blood culture. Hemolytic staphylococcus albus. Five days later hemolytic staphylococcus albus. Five days later no growth. Operation.—Osteotomy drilled. Arthrotomy fifty-four days later; sequestrectomy; incision and drainage; sequestrectomy. Immobilized in plaster after first operation. Course.—Prolonged but steady improvement. Result.—Cured. Subsequent History.—Considerable trouble with sequestra. September 19, 1931, Thiersch skin graft with good result. Follow-up.—March 2, 1932, all wounds healed. General condition good. No limitation of motion.

STREPTOCOCCUS SEPSIS

J. J., aged six months, admitted January 15, 1931; discharged March 18, 1931. Diagnosis.—Eczema, Hemolytic streptococcus bacteremia with metastases to bone and soft tissue; acute suppurative osteomyelitis; acute nephritis. Anatomical Diagnosis (autopsy)—Eczema; suppurative arthritis right ankle; bacteremia, streptococcus hemolytic. Abscess of finger, acromial, malleolar, right hip, right trochanteric and inframammary regions. Suppurative adenitis, osteomyelitis of humerus. Chronic peri-splenitis. Broncho-pneumonia. Emphysema of lungs. Symptoms and Findings.—Rash over cheeks for two weeks, spreading over face and scalp. Profuse diarrhoea and vomiting for one week. Parents luetic. Temperature $103\frac{1}{2}^{\circ}$ on admission; acute otitis media. January 26—

fontanelle full; spinal fluid negative. January 27, right ankle drained; hemolytic streptococcus. January 30—blood culture, hemolytic streptococcus. February 2, proximal phalanx of left index finger drained; hemolytic streptococcus. February 4, abscess of shoulder drained; hemolytic streptococcus. February 7, erysipelas of left buttock and thigh; abscess of ankle drained; hemolytic streptococcus. February 11, five cubic centimetres erysipelas antitoxin. February 13, erysipelas faded. February 14, abscess of parotid region. Right thigh swollen; hip motion restricted. February 15, abscess of elbow drained. February 21, right hip drained; hemolytic streptococcus. March 3, abscess of knee and of thoracic wall drained; hemolytic streptococcus. Became steadily worse and died. X-ray Findings.—Osteomyelitis proximal metaphysis of left humerus. February 16 osteomyelitis of metaphysis of femur. Destructive changes present in proximal portion of right radius and ulna. Operation.—Multiple incision and drainage. February 3 transfusion 100 cubic centimetres whole blood. Result.—Died.

F. S., aged fifteen months, admitted December 27, 1931; discharged January 27, 1932. Diagnosis.—Acute suppurative osteomyelitis of humerus (hemolytic streptococcus). Symptoms and Findings.—December 25, sudden onset of irritability and fever. Tenderness of left arm. Temperature 104°. December 27, definite weakness of left arm; admitted as possible poliomyelitis. Physical Examination.—Left arm painful below shoulder. Spinal fluid negative. December 28 temperature 105°, swelling and slight redness with firm mass felt along outer side of mid-humerus. Blood culture, December 28, hemolytic streptococcus. X-ray Findings.—December 28, no bony changes, January 23, considerable involucrum. No sequestrum. Operation.—Osteotomy. December 29, pus from bone, hemolytic streptococcus. Course.—Uneventful. Result.—Cured. Subsequent History.—None. Follow-up.—March 3, 1932, wound soundly healed. Free motion of arm.

W. H., aged nine months, admitted March 19, 1930; discharged April 11, 1930. Diagnosis.—Bronchopneumonia (group undetermined), hemolytic streptococcus, bacteremia with metastases, acute osteomyelitis of humerus, suppurative arthritis of shoulder. Symptoms and Findings.—Admitted with diagnosis of bronchopneumonia and possible poliomyelitis (later excluded). March 20, definite signs of arthritis of shoulder-joint. Blood cultures, March 19, 21, 23 and 24 grew hemolytic streptococcus. March 26, negative. X-ray Findings.—March 20, evidence of bone involvement of upper humerus. Operation.—March 24, arthrotomy; pus—hemolytic streptococcus. Transfusions on March 20, eighty cubic centimetres; March 21, ninety cubic centimetres; March 22, eighty cubic centimetres; March 24, eighty cubic centimetres; April 4, eighty cubic centimetres. Course.—Following arthrotomy, shoulder lesion promptly healed. Temperature flat for seven days. Good motion of joint. Blood culture negative. Result.—Cured. Subsequent History.—Readmitted April 23, 1930, had arthritis of left hip with dislocation. Joint explored. No pus found; no sequestra. Hip reduced and maintained. Developed measles and discharged June 18. Follow-up.—Motion good in both shoulder and hip-joints. August 17, no deformity. Stands but has not walked (fourteen months old). No further follow-up; family cannot be found.

L. D., aged four months, admitted January 17, 1930; discharged March 15, 1930. Diagnosis.—Acute suppurative arthritis of hip- and shoulder-joints; furunculosis; acute otitis media; bacteremia with metastases. Symptoms and Findings.—Fever; crying as if in pain for five days; swelling of left thigh for three days. Temperature subsided after drainage of hip but rose again two weeks later and shoulder became swollen; drained; developed severe furunculosis. These were drained and patient given autogenous vaccine. January 18 and 21, blood culture, hemolytic streptococcus. February 12, blood culture negative. X-ray Findings.—January 18, 1930, considerable widening of the joint space of left hip with swelling of soft tissues of left thigh. Appearance suggestive of purulent arthritis. November 25, 1931, lateral dislocation of head of left femur. No evidence of osteomyelitis. Operation.—January 18 arthrotomy of hip; twenty cubic centimetres pus—hemolytic streptococcus. February 4, arthrotomy of shoulder—ten cubic centimetres

MAGGOTS AND OSTEOMYELITIS

metres pus. January 21, transfusion, ninety cubic centimetres whole blood. Course.—All wounds healed at time of discharge. Result.—Improved. Follow-up.—November 18, 1931, walks with slight limp. Has $\frac{1}{4}$ inch shortening of leg. Arm well healed with good function of shoulder. Referred to Orthopedic Hospital for reduction of dislocated hip.

S. F., aged four months, admitted April 18, 1930; discharged June 14, 1930. Diagnosis.—Abscess of lateral femoral region; hemolytic streptococcus bacteremia with metastases. Acute suppurative osteomyelitis of upper extremity of tibia. Acute arthritis of knee-joint. Measles. Symptoms and Findings.—Fever, rhinitis, irritability, for two weeks. Swelling of left thigh and edema of leg for one week. Temperature 101° - 102° . Blood culture on admission showed hemolytic streptococcus. X-ray Findings.—Purulent osteo-arthritis of tibia; probable epiphysitis of upper tibial epiphysis. Operation.—April 19, drainage of thigh abscess. May 13, arthrotomy left knee. Both cultured hemolytic streptococcus. Course.—Following drainage of thigh abscess, erysipelas developed in wound; 15,000 units antitoxin given. Result.—Infection cured. Some residual knee contracture. Subsequent History.—Developed measles, June 12. Follow-up.—Some flexion contracture of knee. All wounds well healed.

A. D., aged ten months, admitted July 31, 1930; discharged September 2, 1930. Diagnosis.—Acute suppurative osteomyelitis of lower extremity of fibula; hemolytic streptococcus bacteremia with metastases. Symptoms and Findings.—Fever for five days; one convulsion; for four days temperature was 104° - 106° . For three days had a painful left leg. Both blood and wound cultures showed hemolytic streptococcus. August 13 blood culture showed no growth. No X-ray findings were reported. Operation.—Incision and drainage. Bone drilled and wound packed with vaseline gauze. Course.—Normal; discharged thirty-two days after operation with slight drainage. Developed furuncle on hand ten days after operation with culture showing hemolytic streptococcus. Result.—Improved. Follow-up.—February 15, 1932, wound well healed. Has been treated at Orthopedic Hospital where X-rays were said to show small sequestra.

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FRACTURE OF THE NECK OF THE FEMUR

CLINICAL CRITERIA IN PROGNOSIS

BY KELLOGG SPEED, M.D.

OF CHICAGO, ILL.

THIS report seeks to expose practical points in the treatment of fractures of the neck of the femur, laying stress on two factors based on a study of clinical and laboratory material which may be used as criteria in prognosis. Intertrochanteric fracture of the femur is excluded, because it is not similar in reaction and result and because it was covered in a report made by me after a study of 120 cases.

Briefly, to recall the orthodox steps in treatment of fractures of the neck of the femur, based largely on Whitman's work in 1890, we expect to put the patient through manœuvres which include pulling the leg out to full length, inverting it to bring bony contact between fractured surface of the head and trochanteric portion, abduction to the fullest extent to jam the bony surfaces together and to hold them impotently in that reduced position, the whole followed by immobilization in a proper dressing, usually plaster-of-Paris, until bony union has been secured, and motion, weight-bearing and functional use may follow.

It is possibly needless to vouch for the simplicity and potential accuracy of this accepted method of treatment. Various collections of so-called end-results in series of patients thus treated are recorded in the literature. From the Massachusetts General Hospital we learn that there are 60 per cent. of successful outcomes from this treatment in a small group of cases. Whitman himself, Hey-Groves, Campbell, Stern and others give grouped results with and without making statements covering the varying percentages of cures. In spite of really great advance in the treatment of this major peripheral fracture of the skeleton some men have persisted in studying the situation further, not necessarily on account of the approximately 40 per cent. of untoward results, but to better fracture-treatment situation as a whole and to stimulate renewed interest and actual exposure of just what goes on during the healing or failure to heal of a fracture of the neck of the femur. Among other contributions have been those of Reggio, Santos and Phemister. Two of my own contributions were in 1924 and 1928.

The two points I wish to bring out now as clinical criteria in prognosis which may help also in treatment can be employed whether the method applied has been nonoperative or operative, provided the customary rules of fracture treatment have been followed, namely, apposition, rest, immobilization.

These two factors are: (1) Has the head of the bone retained its vitality or is it undergoing aseptic necrosis with or without substitution of bone;

(2) are the supporting bony trabeculae in the head and neck reforming to give proper weight-bearing support and lasting function. The second factor undoubtedly depends on the first; the two taken together afford a clear expression as to the prognosis of union and the future use of the leg.

After fracture of the neck of the femur a certain amount of aseptic necrosis of bone, followed by invasion with osteoid tissue, develops across the fracture plane and extends backwards into the cancellous bony tissue of both fragments for a varying distance. If the fracture is early reduced and held in position as in the orthodox treatment, does bony union always follow? Unfortunately, no. Union may not follow even when the apposition or reduction is enhanced by natural impaction or Cotton's artificial impaction, or by open operation which freshens bony surface and insures exact apposition under the surgeon's eye, or is supported and possibly physiologically aided by a bone transplant or drill holes inserted across the fracture plane. So much seems to depend on the viability of the head, its retention of sufficient blood supply from its periosteal, capsular or ligamentum teres vessels to maintain itself alive. This principal fact is necessary to insure stable and lasting bony union to the trochanteric fragment, the avoidance of flattening of the head, ununiting fracture, and delayed breaking down of the bone with aseptic necrosis. If this blood supply is insufficient various parts of the head, deprived of nourishment, will die. Such dead heads retain their original density and bear a striking contrast in the röntgenogram to the surrounding bone of pelvis and femur which undergoes loss of calcium salts incidental to the enforced rest from use after fracture and immobilization. The head dying or dead shows a deeper X-ray shadow in those parts affected. It may be possible for a vigorously vascular trochanteric fragment to build up osteoid tissue and really unite with a head, dead for the most part. But this union will not be stable nor lasting when it is subjected to the test of functional use and weight-bearing.

If the head fragment dies, undergoes aseptic necrosis in whole or in part, a reestablishment of vascular supply, a carrying in of new vessels and an absorption of dead bone and a rebuilding of new bone may eventually furnish the patient with a viable, well-formed bony head which will tolerate all the requirements of use. That process takes time and leads to the second or mechanical point I wish to make.

After any fracture followed by annealing callus formation a rebuilding and refining of the callus must ensue before a final stage of healing of the fracture is established. Nowhere is this slower, more necessary nor more important than in the neck of the femur. This rebuilding of newly formed callus or bone from osteoid tissue in the neck of the femur is shown by a realignment of the bone trabeculae which are the underlying bridge work of the bony structure which give the support required for the stresses of use. Long after the deposit of calcium salts as callus or new bone has reached an end stage, this refining and trabecular rebuilding must go on until the

FRACTURE OF THE NECK OF THE FEMUR

architectural structure of the bone in the neck of the femur assumes mature form and is capable of carrying on the work of use. One can study this architectural arrangement in the normal neck of the femur to familiarize one's eye with the directions of the trabecular lines and thus be prepared to compare with the normal the process as shown in the röntgenogram (Figs. 1 and 2) of a given case after a fracture of the neck of the femur. Once the trabeculae are thoroughly and maturely reformed, the observer is confident that the bone will stand use, and that weight-bearing can safely be undertaken by the patient. No nonunion, no ununiting of the healing frac-



FIG. 1.



FIG. 2.

FIG. 1.—Autopsy specimen of impacted fracture of the neck of the femur three weeks after the accident. The cartilage on the head shows no gross change, the bone in the head appears uniformly dense and its viability is indeterminable. At the fracture plane evidences of blood extravasation, revascularization are showing. In the trochanteric portion of the diaphysis are evidences of hyperæmia and blood extravasation. All vascular and bone changes in these areas are slow in development.

FIG. 2.—X-ray film of the specimen shown in Fig. 1 three weeks after fracture. The plane of fracture is slightly impacted. The well-defined trabeculae in the head mesh into those of the diaphysis which are far less well defined, but angulate sharply at the level of contact. In the diaphysis is apparent bony absorption, extending up toward the plane of fracture. At the exact plane of fracture appears heavy bone shadow as if the bone were dead and starting to undergo absorption. The deep clear shadows of the head might lead one to suspect three weeks after fracture that the head was largely dead.

tured neck of the femur is going to take place in the face of that finding when increasing graduated use and weight-bearing demonstrate no röntgenological change in trabecular alignment. X-ray control (Figs. 3 and 4), however, at suitable short intervals must depend on the reaction of the bone within itself to the physiological requirements it has to meet. Hence factor

two, this trabecular realignment, must depend on factor one, a retained vitality and blood supply of bone in the head and fracture region.

Chandler, of Chicago, has studied the blood-vessels of the ligamentum teres to find that in 112 ligaments removed from sixty-five cadavers all showed definite blood-vessels in this ligament, some as large as 1.3 millimetres in diameter. On section, four of the ligaments were classed as avascular because only very small vessels were present; eight ligaments contained a large number of small vessels, thirty-six ligaments contained vessels less than half a millimetre in diameter. A group of forty-eight ligaments contained vessels from one-twelfth to one millimetre or greater in size. The

ligamentum teres vessels in every case were shown to have connections with those in the head of the femur and it must become an accepted surgical fact that these vessels are normal, constant, and



FIG. 3.

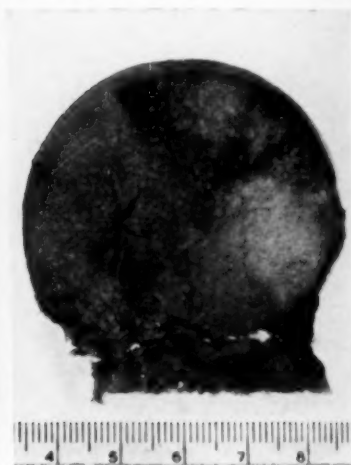


FIG. 4.

FIG. 3.—Another autopsy specimen four and a half months after fracture. The dense shadow in the centre of the head leads to the impression that bone there is dead. Union at the fracture site is not apparent. There is great absorption of calcium on the diaphyseal side. Loss of bony shadow on the edge of the head leads to a supposition that bone absorption or replacement is going on there from blood supply furnished from ligamentum teres vessels.

FIG. 4.—A wafer section through this head and fracture shown in Fig. 3 four and a half months after fracture. The whitish thick areas in the head represent dead bone, deprived of blood supply. The darkened areas represent invasion by blood-vessels and replacement or absorption of the old bone. The fracture is plainly ununited, the bony trabeculae across the fracture in the neck have not reformed at all.

important in sustaining viability of the head of the femur (Figs. 5 and 6) after fracture along with the other sources of blood supply to the head and neck arising from the capsules of the joint, the periosteum or the extended blood supply of the diaphysis originating from the superior nutrient artery of the femur.

Certain other factors must be considered clinically in discussion of neck fracture.

FRACTURE OF THE NECK OF THE FEMUR

(1) The trauma of fracture may tear off the ligamentum teres or tear and injure its vessels by stretching or compressing without true rupture of the ligament so that the blood supply coming along this avenue is permanently interfered with. Traumatic thrombosis may be present.

(2) The trauma of fracture may likewise interfere with the vitality and nutrition of the cartilage on the head of the femur by pressure, later to cause death of the cartilage and invasion by the underlying bone.

There may consequently be certain heads of the femur doomed to die (Figs. 7 and 8) after fracture of the neck despite any line of treatment based on the integrity of the blood supply of the head acquired through the



FIG. 5.



FIG. 6.

FIG. 5.—Another autopsy specimen three months after fracture of the neck. The fracture has not united although impacted. The head appears quite viable. Some trabeculae seem to be lining up on the inner side of the neck but they are not in true alignment. There is here also great loss of calcium in the diaphyseal portion of the bone.

FIG. 6.—Autopsy specimen over two years after fracture of the neck. A true union has followed and one can see a complete restoration of the lines of supporting trabeculae of bone from the diaphysis up into the live head.

vessels of the ligamentum teres. The other sources of blood supply may be too scanty or may be so interfered with by fracture that aseptic necrosis of the head is inevitable, the balance of vitality in the head from the various precarious sources of supply being just sufficient to maintain nutrition under normal untraumatized conditions.

We find clinically that some heads of the femur in elderly people do break down to undergo aseptic necrosis and fragmentation in the absence of known fracture or recognized specific (but not chronic) trauma. In Legg-Perthes disease in adolescents the head likewise becomes necrotic and dead, definite trauma apparently not entering as a causative factor. In many cases of

congenital dislocation of the hip, the nucleus of the head, which may be small but not necrotic, while the dislocation is in existence, takes on new growth and may reach mature size after reduction followed by the stimulation of normal use. In such instances the ligamentum teres, though stretched, has not been torn; it may be found at operation for open reduction of these dislocations and its vessels function.

On this basis the operation devised by Hey-Groves for pegging the head of the femur onto the diaphysis via the open path of the fovea by first removing it entirely from the acetabulum and cutting away the ligamentum teres seems absolutely unwise and undesirable. Any unions after such procedures must be by chance; they may be studied long enough to represent union of the neck to a dead head which ultimately breaks down and becomes fragmented in a large proportion of the cases.

In operative treatment of fracture of the neck by insertion of an autogenous bone peg from the trochanteric side the exact angle and position of

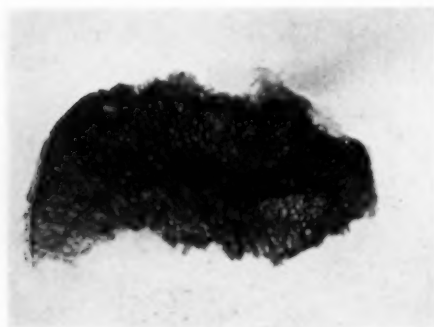


FIG. 7.

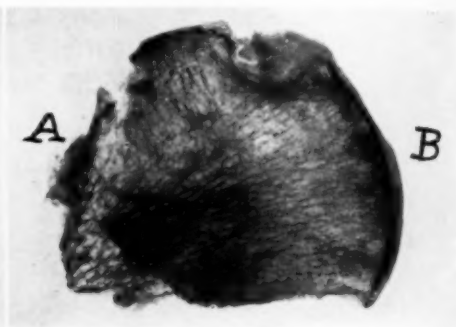


FIG. 8.

FIG. 7.—X-ray study of wafer-section head of femur removed eleven months after fracture of neck of femur in the performance of a reconstruction operation. The loss of cartilage by erosion, the loss of underlying bone substance, the uniform deep density of the trabeculae in the head and the absorption along the edge of the uneven fracture plane make it evident that the head is dead and little or no effort at revascularization of it has occurred.

FIG. 8.—X-ray study of wafer section of head of femur sixteen months after fracture when head was removed for a reconstruction operation following nonunion with much pain when weight-bearing was attempted. The fovea is plainly seen with evidence beneath it of bone absorption and replacement. The replaced bone is lighter in calcium shadow and its spaces are wider, its trabeculae finer in shadow. In areas on the head the cartilage (A) is eroded and loosened with some broken-down and dead bone beneath. In other areas of the head (B) the cartilage seems still viable with dead bone just beneath. Some of the head in lighter shadow is evidently replaced by newly formed bone, apparently taking blood supply from the fovea and near the fracture plane are found old deep shadow-producing trabeculae of dead bone of original density of the head as of the day of accident. Apparently no effort at union with the diaphysis but on the whole considerable replacement of the head by new bone. A partially alive head.

the bone peg may excite discussion. If it enters the head fragment in such a manner that it points directly into the fovea or the path of the vessels of the ligamentum teres entering via the fovea, may it shut off the scant blood supply of the head as would the peg inserted from the head side through the open fovea. For the average surgeon it would hardly be possible to avoid this direction of the peg with any certainty, even with the help of fluoroscopical control, and he would be both lucky and satisfied to get the peg well into the centre of the head.

Other points of greater refinement, concerning the function of autogenous

FRACTURE OF THE NECK OF THE FEMUR

bone pegs and the healing formation of bone after fracture must be considered in this matter. There is no known proof that under the normal condition of insertion of an autogenous bone peg any increased blood supply of the head of the femur results or that pegs inserted so as to avoid the fovea region in a series of cases, lead to sure bony union and not to a breaking down of the head fragment. If, therefore, after this fracture we feel that we should preserve every known bit of blood supply in the region, why insert any bone peg at all, especially in fresh fracture? The bone transplant may be of use as a fixation agent, the freshening of the bone surfaces of the neck and head may be the largest factor in providing new and lasting blood supply with the subsequent introduction of osteoid tissue, callus formation and eventual reconstruction into trabecular bone. I cannot see that any

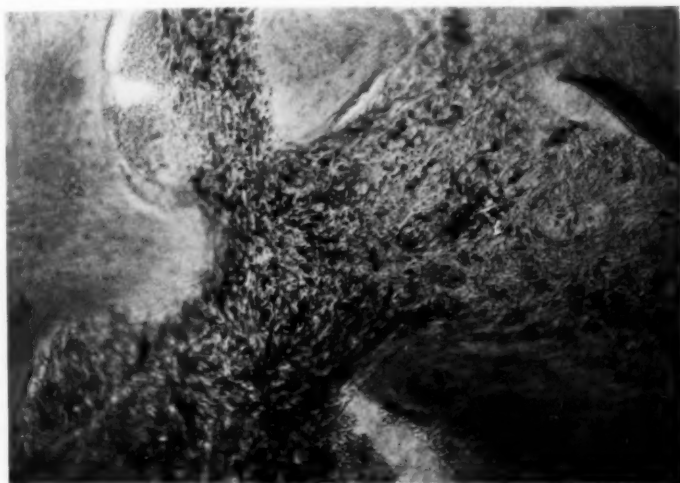


FIG. 9.—Photomicrograph of fibrous replacement of dead bone of the head in another specimen removed for reconstruction operation on account of dead head and nonunion. There seems to be no effort at new bone formation even under the microscope.

modification of the technic of bone transplant, insertion or reposition as suggested by Jones in trochanteric transplantation affects the underlying physiological principles.

A microscopical study of heads of the femur which we have removed at varying periods of time (Figs. 9, 10, 11 and 12) after fracture along with study of post-mortem specimens recovered months and years after fracture seem to show that the vessels incoming via the ligamentum teres are dilated after fracture; they lead to the bringing in or development of osteoid tissue which is to form new bone. Old dead bone can be seen undergoing absorption but there is no positive evidence that new bone formed in the immediate vicinity necessarily takes its calcium supply from disintegration of the dead bone.

Can we say, therefore, that a bone transplant in the neck of the femur offers new bone or increases the blood supply or offers any physiological

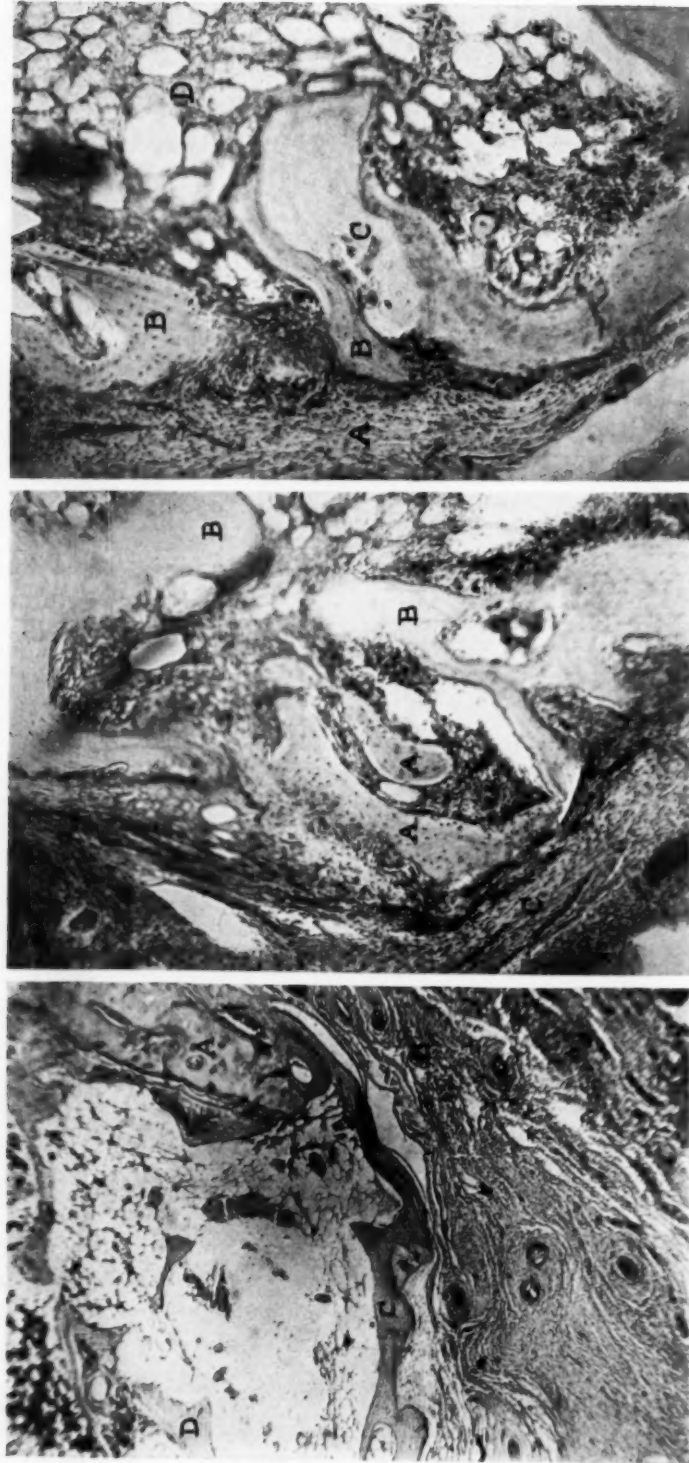


FIG. 10.

FIG. 10.—Photomicrograph of section through the fovea region of the head shown in Fig. 8 (sixteen months after fracture). At A is the cartilage of the head with many viable cells. Below that at B the ligamentum teres attachment dips into the head carrying its fibrous tissue and blood-vessels. Dilatation of these vessels may be seen. At C is found newly laid down bone along the edge of the fibrous osteoid tissue fed from the fovea vessels. D is dead bone in the head not yet absorbed.

FIG. 11.

FIG. 11.—Photomicrograph of section of another area deeper down in the head showing the inspreding vascularization of osteoid tissue. A is newly formed bone; B old dead bone; C the fibrous replacement with osteoid tissue. At A, B is seen newly formed bone; at C old dead bone. There is no union between the head and the neck of the head.

FIG. 12.

FIG. 12.—Photomicrograph of section near edge of the head showing the replacement of fibrous tissue by osteoclasts; at D washed-out dead bone. The bone of the head is vigorously progressing from blood supply brought in through the ligamentum teres vesicula via the fovea. There was absolutely no union across the neck fracture.

plete reduction of fracture of the neck of the femur in adults the same has resulted. In perfectly clean instances of autogenous bone pegging of fracture of the neck of the femur with apparently good result, the same disintegration, aseptic necrosis, flattening of the head and cartilage-shedding process has been found years later.

It is then necessary to assay the fractures of the neck of the femur from a little different standpoint if we wish to get clearer indications for reconstruction operations and reliable statistics of the percentage of final cure. Trustworthy statistics can be obtained only when all cases are studied röntgenologically for years.

For purposes of criteria in prognosis that we may count upon to assure both patient and ourselves, these two clinical findings revealed by the röntgenological study may be taken as guides. Final results want years of observation.

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